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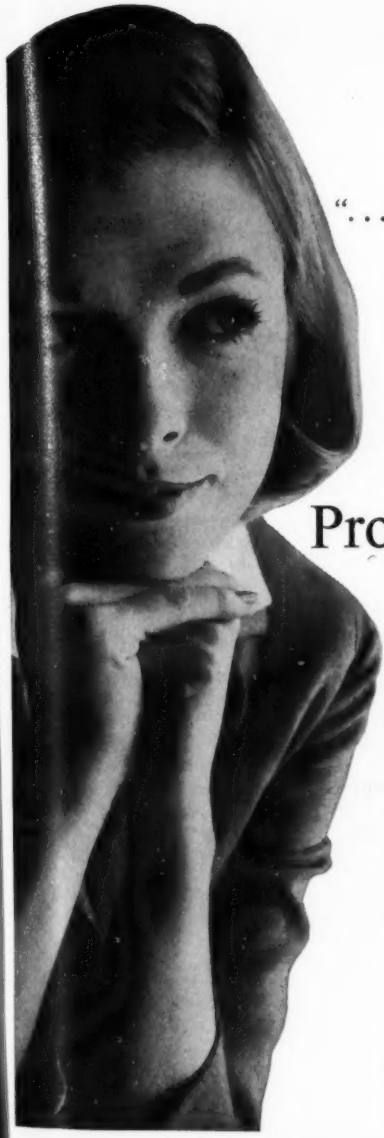

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1. Schwartz, H.A.: Editorial, Minnesota Medicine *42*:1279, 1959.

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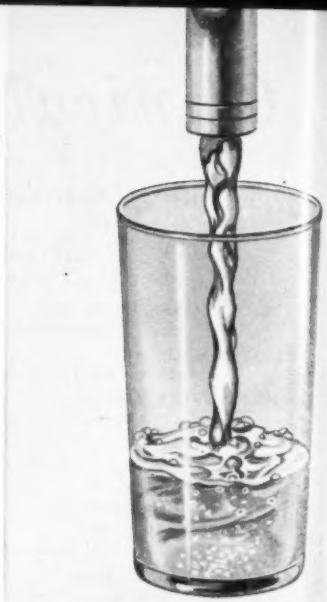

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Ulcers in Paradise

JOSEPH FRANKLIN MONTAGUE, M.D., F.I.C.S.,*
New York, New York

►*Although the isolated culture discovered by anthropologists in the interior of New Guinea was favored by fertile land and an eternal spring climate, the inhabitants suffered from diseases. Their study offers an opportunity for genetic research and presents an argument for psychosomatic medicine.*◄

The poet Milton wrote of *Paradise Lost* and *Paradise Regained*, but it remained a poet's dream until James Hilton wrote his novel describing a mythical Shangri-la right here on earth. Since then numerous explorers have delved into previously unexplored regions and have, from time to time, announced the *exact* location of what they considered to be a true Paradise on Earth. The nearest approach to such a location in my opinion was that made by two Australian lads, who, in 1954 burst into the hitherto unknown and unsuspected Waghi Valley in Central Papua on the Island of New Guinea.

Here, on the largest island in the largest ocean—just northeast of Australia—is a huge range of wild rugged mountains which by virtue of their precipitous sides and dense jungle growth had never been penetrated by white men. Indeed, the very existence of any human being in the interior was not even suspected. Lured by tales of its inaccessibility and the hope of finding precious metals, minerals or oil, the Leahy Brothers hacked their way through the jungle, scaled sheer mountain sides and blundered into and through a small fault or break in the mountain wall to enter into a beautiful, broad, fertile valley such as they never dreamed of finding.

Here they found an abundance of luxurious vegetation, a myriad of beautiful flowers and tall stately trees through whose branches flitted brilliantly plumaged birds. Chief among these

*Fellow, American Public Health Association, American Anthropologic Association, American Geographical Society, Royal Society of Health (London). Member, Circumnavigators' Club.

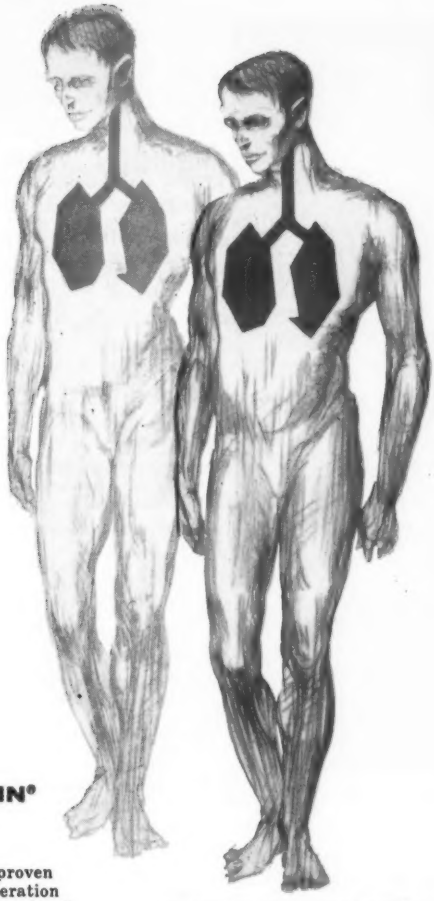
was the beautiful Bird of Paradise. But there were also beautiful colored parrots, macaws and cockatoos. Surely they were gazing upon scenes of the primeval!

Much to their amazement, they also noticed evidences of cultivation, of spaces in the forest which indicated an artificial arrangement of planting. Then, there were well-ordered gardens and small farms to be observed, criss-crossed like the face of Mars, with man-made canals. As they progressed further, they saw huts evidently used for living and others which were clearly recognized by an anthropologist as a sing-sing hut, a place where tribal gatherings were held and ceremonies performed. In time, the explorers were privileged to see some of the inhabitants when natural timidity and caution had been overcome by the fact that the exploring white men apparently were not intent upon mischief. This was the first time that they had ever seen a white man. Conversely, this was the first time that white men had ever viewed this segment of society.

No stranger fragment of humanity was ever brought to the attention of civilized men. Here were people of evident Melanesian stock, who were living, and apparently had been living, in the most primitive style imaginable. They wore no clothing except a colorful and ponderous feathered headdress made from the plumage of the birds I have described. Many wore no other articles of clothing. Some wore loin belts or ornaments of a most scanty nature. They carried stone implements and indeed were living in a stone age culture. The whole valley has a population of perhaps 100,000 people, grouped in small clans or tribes and having one thing in common—a constant inter-necine warfare.

It was quickly learned by those who came later with the Leahys to study and govern the land, that although this was land of eternal spring—a fertile land which would grow any desired food, a land that bathed in wholesome sunshine and good pure air—it was nevertheless a land pervaded with all manner of diseases.

Being a specialist of diseases of the stomach and intestines, these were naturally the main source of my interest, but in the course of my investigations I also encountered skin diseases such as yaws, fungus infections and leprosy, and eye diseases such as trachoma and blindness. Some of the diseases encountered have yet to acquire classification in a medical textbook. As one such



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situation, I mention the "laughing death," a disease characterized by one long bout of laughter, often of six to nine months duration, but with an invariable ending—death. In the five years during which its existence has been known, and despite skillful investigations both by microscope and autopsy, nothing definite is known. Reports invariably end "no specific lesions."

Of course the sad part is that no remedy is known. High potency vitamins and antibiotics have no effect. In fact, no known medicine (and most of them have been tried) has the slightest effect on the course of the disease. Curiously enough, it is limited to the Foré Tribe which live high on a mountain ridge, and to a much lesser extent their immediate neighbors. The disease starts as a twitching of the muscles of the arms and face. Bodily weakness develops, progressing to such an extent that the victim finally cannot even walk. Trembling of the body, as seen in paralysis agitans (common palsy) becomes marked as the disease progresses. The patients eventually die from malnutrition as they become unable to eat. Extensive research is being carried forward by the Rockefeller Foundation and by the National Health Institution. So far the only conclusions have been that apparently it is due to some defect in the genes which is transmitted from parents to children. Dr. R. F. R. Scragg of Port Moresby regards it as an outstanding medical problem.

Aside from this and other exotic miseries which the Papuans share among themselves, there are some good old-fashioned civlized disease, too (in fact, some that you would be willing to wager couldn't happen in a "Paradise" such as this). We usually think of the primitive savage as a carefree, happy-go-lucky individual, healthy and devoid of the usual diseases of mankind. Certainly, in a land like this, far removed from the maddening throng, committed to no deadlines or commuter schedules, and comfortably devoid from income tax collectors, one would hardly expect to find an ulcer in an acre.

Yet quite to the contrary, a brief sojourn with these people revealed the highest rate of peptic ulcers ever found in any community, higher by far than in our own cities. So, too, were cases of colitis and various other nervous functional disorders. Confronting such a situation one is necessarily tempted to ask, "What on earth do they eat that would give them such an abnormally large share of stomach ulcers?"

This was the question put to me when discussing this with Papuan Administrators. I recalled a phrase which I had coined and used in my book "How to Overcome Nervous Stomach Trouble." In this book I said "Ulcers are not what you get from what you eat *but from what is eating you.*" Working on this principle, I soon found abundant reasons for ulcers in "Paradise." I found it in the most outstanding set of taboos I had ever heard of in any anthropological studies. I found it in the existence of an almost unbelievable, sizzling sex hostility —literally a sort of "boy hates girl" situation in which the girls actively reciprocate.

It all starts this way: At the age of 7, all male children are taken from their mothers and given a ceremonial washing in the nearest lake or river. The object of this bath is to remove all traces of formal contact with the mother and henceforth the boys live with the men and they live forever apart from the women. (Well! almost.) Then long grasses are forced down the children's throats to elicit vomiting. This is done to get rid of any food which may have been touched by a woman. From then on they are fed by and live with the men of the village in a special house which is set apart for them. Naturally, this implies that men and women live apart all of their married life.

Such a condition can be productive of emotional tensions to say the least, but there are still further refinements to the theme of taboo. At the age of puberty, the boy is subjected to further ritual, including scarifying his genitals. The object of this is expressed in pidgin English "Lusem blut bilong mumma." In other words, the object of the ceremony is to get rid of the mother's blood. By now, and from that time forward, the young boy believes, and is encouraged to believe, that all girls are "bad medicine" and that the less he has to do with them the better it will be for him.

But, of course, marriages must happen if the tribe is to continue and have warriors. Hence women are tolerated, allowed to till the fields, to seek out and bring the food. However, the men insist upon preparing their own food and take every opportunity to express their contempt of the female and the superiority of the male. No better example of this can be given than that of the marriage ceremony. When marriage finally does take place the custom dictates that the bride seat herself in front of a hut with her right leg extended. Then the bridegroom approaches

and shoots a small arrow into her right thigh to show his superiority. He then draws the arrow out and they enter the hut for the honeymoon. I am inclined to think that instead of living happily ever after, it might be more truthfully said that they live *unhappily* ever after. In any event, you can see that this hardly constitutes a promising basis of domestic harmony. Furthermore, a little later that evening the bridegroom *goes home to sleep—with the men*—and thereafter only sees his wife on occasion!

I have spoken of the men insisting upon preparing their own food. Considering the treatment they give the women, this custom certainly seems to have a sound basis, since people do die of food poisoning. Add to this the fact that sometimes one of the wives that he marries is a girl whom he took from a neighboring village along with her husband's head, and you can see how careful a man has to be with his calories. If all this does not add up to an ulcer by now, let me throw this in for good measure:

Since these people are head-hunters and cannibals, they feel it only fair to retaliate when the head is taken off the shoulders of one of their friends and they frequently drop in at the most unexpected times to collect a head or two of their own to balance the account. Under such circumstances, it is no doubt difficult to keep one's head both figuratively and literally. In fact, they have the nervous system of the A string on a well-tuned violin and are apparently always on the verge of an emotional explosion. Small wonder, then, that so many inhabitants of "Paradise" have ulcers!◀

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Diagnosis and Treatment of Acute Myocardial Infarction

MICHAEL BERNREITER, M.D.,* *Kansas City, Missouri*

►*Of tests available for the diagnosis of acute myocardial infarction, electrocardiogram is the most conclusive. Anticoagulant drugs, a significant advance in therapy, should be started as soon as diagnosis is made and controlled by frequent prothrombin time estimation. Quinidine is given to prevent arrhythmia.*◄

The diagnosis of myocardial infarction depends particularly on chest pain, appearance of shock and characteristic electrocardiographic findings. Of the laboratory tests, estimation of transaminase is quite helpful. It is important to remember that elevation of serum transaminase is found in other conditions with tissue destruction, especially in liver disease, also that the transaminase in myocardial infarction may be elevated only for the first three days of the acute phase.

Chest pain in itself is no definite evidence that infarction has occurred, as this symptom is found in many other conditions (arthritis, Tietze's syndrome, neuritis, dissecting aneurysm, pulmonary diseases, etc.). Of all laboratory tests available, the electrocardiogram is by far the most conclusive. I doubt that a patient can have an acute myocardial infarction without showing some changes in serial electrocardiograms.

*Dept. of Electrocardiography, St. Mary's Hospital, Kansas City, Missouri.

Treatment

The treatment of acute myocardial infarction is designed to reduce the work of the heart, to relieve pain, to overcome shock and cardiac failure, and to prevent or treat cardiac arrhythmias and thrombo-embolic phenomena.

To reduce the work of the heart, bed rest is essential. It has been shown that at least three weeks are necessary for development of collateral circulation and six weeks to convert the infarct into a good scar. Relief of pain in the early phases of an

acute infarction is an absolute necessity as persistent severe pain will bring on or increase the state of shock. Pain and apprehension are best relieved by morphine sulfate gr. ¼-½, repeated as necessary. Severe pain in acute myocardial infarction is usually of rather short duration (36 to 48 hours), so the danger of habituation is not great. The myocardium, shut off from blood supply by a thrombosed coronary artery, will usually die within 48 hours and dead muscle can suffer no pain.

The treatment of shock after infarction has to be instituted early. A patient who is allowed to remain in shock for more than four hours is beyond hope. Levophed is perhaps the best pressor amine at our disposal. It is given intravenously in 500 cc. of glucose or saline. Under this management the patient should be watched carefully, the blood pressure, taken every five minutes and the speed of Levophed administration adjusted to the blood pressure. Levophed, if accidentally infused into the tissue, may produce a slough. Even if the needle remains in the vein, prolonged administration of levophed can produce severe capillary spasm and gangrene of surrounding tissue. The first manifestation is a blanching in the area of injection. One should then reinsert the needle in a different area, and recently we have been able to prevent tissue gangrene by regitine injections into the damaged tissue.

The most significant recent advance in the treatment of coronary occlusion is anticoagulation therapy. Almost all types of thrombo-embolic complications, rather common occurrences before anticoagulation drugs, can now be prevented, and as a result the mortality rate has been decreased. It is important that anticoagulation therapy be started as soon as the diagnosis is made and that its administration be controlled by frequent prothrombin time estimation. The prothrombin time of the patient so treated should be 2½ to 3 times the control. If hemorrhages would occur, vitamin K will reduce the prothrombin time to more normal levels in a few hours.

Some of the patients with myocardial infarction die suddenly as a result of cardiac arrhythmias. It is our custom to administer quinidine, grs. 3, t.i.d. to all such patients in the hope that the arrhythmias may be prevented. Cardiac arrhythmias of all sorts are a dangerous complication in acute myocardial infarction and one should make a real effort to control them. Frequent ventricular premature contractions may respond to pro-

caine, 1 gm. every four hours.

Diet the first few days after infarction consists of liquids only and as the patient improves his caloric intake will be increased, but it should be limited particularly in patients who are overweight. The cholesterol intake is permanently reduced. To prevent deficiency a multivitamin preparation is usually given once or twice daily.◀

Vesico-Urethral Reflux in Children

It has not been determined whether this regurgitation of urine from the bladder into the ureter occurs in normal persons. The condition is usually associated with some urologic disease, its expectancy in children with such complaints being about 10 to 12%. Frequency of diagnosis depends on the thoroughness of the examiner. The examination is started by passing a small catheter into the bladder and injecting 60 to 100 ml. of sodium iodide solution. The catheter is then removed and the child instructed not to void for 20 to 30 minutes, at which time a cystogram is taken. If reflux is not demonstrated in the delayed cystogram, an exposure is made while the child is voiding. In the very young child it may be difficult to obtain a good voiding film, in which instances the same result can be obtained if the child is made to cry.

Every child with repeated urinary tract infections, residual urine, unexplained fever, vague abdominal complaints or flank pain, should be studied by cystography. In most instances symptoms of infection are present. Although infection may cause loss of elasticity of the intramural catheter (thereby destroying the valve-like action of this segment) congenital anamolies, neurologic bladder disorders, or trauma to the intramural ureter incident to surgery may also be responsible.

Untreated, this condition may lead to renal destruction, either from increasing back pressure or from repeated infections. Unrecognized, it may represent the explanation in many cases of adults seen in the terminal stages of chronic pyelonephritis. Measures directed at eradicating the cause or contributing factors should be tried first. If these fail reimplantation of the ureters becomes a necesssity to prevent renal injury or damage.

Politano, V. A., *J. South Carolina M.A.*, 417-421,1959.

Psoriasis: Treatment of Varied Local Areas with Three New Topical Preparations

LOUIS WEXLER, M.D., *New York, New York*

►*Of 74 patients with psoriatic involvement of various local areas, 80% showed satisfactory response to either of three new topical preparations. A coal tar-allantoin ointment proved most effective for treatment of glabrous and intertriginous areas, while a phenol-amino acid oil effectively controlled scalp involvement.*◄

Psoriasis constitutes about 5 per cent of all cutaneous diseases, occurring in 1 to 2 per cent of persons of the white race. The size, distribution and character of the scaling plaques characteristic of this disease are extremely variable, thereby creating the therapeutic problem of treating differently affected and differently responding local areas.

Clinical Study

Three topically applied medications have been used and found useful in 74 patients with psoriasis of glabrous skin, inflamed intertriginous areas and the scalp. Many of these patients had varied involvement and had used a variety of preparations.

A combination containing allantoin 2% and a solution of 2% coal tar in a specially formulated Ringer's solution-soy bean complex gell base* was used in the 61 patients with psoriasis of the glabrous skin. Soy bean complex exerts a non-irritating cleansing action and facilitates contact with the skin, while the antipruritic, keratolytic and keratoplastic action of tar aids in removal of scales and crusts. Allantoin serves to disperse sticky psoriatic crusts and scales, thus promoting regeneration of normal epithelium, cell proliferation and healing.[1] The ointment was applied to the psoriatic lesions twice daily, patients being instructed to take a protein colloid† bath at least once daily prior to its use. The majority of these patients were observed at weekly intervals, a few at two-week

*Altara Gell®, Dome Chemicals Inc., N.Y.

1. Flesch, P., & Esoda, E. C. J., *Ann. New York Acad. Sc.*, 73:989,1958.

†Soyaloid®, Dome Chemicals Inc., N.Y.

intervals. The period of observation was from four to 12 weeks.

Of the 61, 49 (80%) showed fair to excellent results, while 12 (20%) gave evidence of slight to no improvement. In 13 patients the lesions completely or almost completely cleared in less than six weeks. Irritation, burning and itching at the treated sites were noted in two patients.

A combination containing ¼% hydrocortisone alcohol in addition to the ingredients contained in the first preparation (Altara Gell) was used particularly in the treatment of inflammatory psoriasis of the intertriginous areas of the skin.* Twelve patients with psoriasis of the crural areas, scrotum, penis, intergluteal folds and axillae, were selected for this study. Regimen was the same as that for the 61 patients with psoriasis of the glabrous areas. These 12 were seen an average of once weekly. The period of observation was from three to eight weeks. Ten (83%) experienced a satisfactory response, while two showed slight to no clearing. In those cases where itching and burning were present, these subjective symptoms were relieved in a matter of days. No adverse effects were noted.

The third preparation, an oil containing phenol 1.2% in a nonaqueous menstruum and an acylated amino acid (included since there is a disturbed protein metabolism of the epidermis in psoriasis)† was used in the 49 patients with psoriasis of the scalp and adjoining skin margins. Of these 49, 28 were women and 21 men (average age 34 years). These patients were instructed to rub the oil gently into the affected areas, using a cotton applicator. Of these patients, 39 (80%) showed a satisfactory response. Although one patient complained of irritation of the skin after seven weeks use, 48 patch tests were negative.

Illustrative Case

Figures 1 through 4 illustrate the case of a woman of 42 with a history of psoriasis for 20 years.

Discussion

A primary problem in the treatment of psoriasis is the attitude of the patient. The typical chronically affected patient with this disease is a cynical, annoyed and frustrated individual. Another therapeutic problem is the diversity and varying degrees of responsiveness of the areas involved. In management of psoriasis of the scalp, particularly in women with long hair, ointments and lotions applied to the scalp frequently produce excessive greasiness and mat the hair. Such preparations are often un-

*Altara-Cort Gell®, Dome Chemicals Inc., N.Y.

†Sarcophen®, Dome Chemicals Inc., N.Y.

RESPONSE TO *ALTARA GELL* AND *SARCOPHEN* IN A WOMAN WITH A HISTORY OF PSORIASIS FOR 20 YEARS

FIGURE 1

Typical geography of psoriatic, scaly, erythematous skin, widely distributed over the back. Although numerous preparations had been employed in this patient, none had given results which could be considered as thoroughly or uniformly effective.

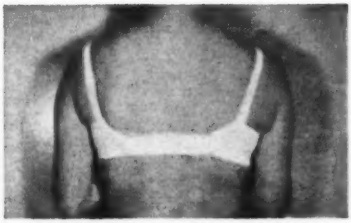

FIGURE 2

Response in the same patient following use of an allantoin-coal tar ointment (Altara Gell) twice daily for a continuous period of six weeks. The entire area appears cleared, and the patient has reported almost complete cessation of itching.

FIGURE 3

The same patient, showing the extent of psoriatic involvement of the scalp. A variety of topical medications had also been employed for this area, but none had produced any more than minimal or temporary relief from scaliness and itching.

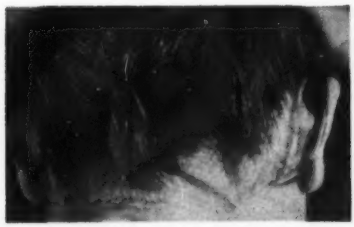

FIGURE 4

Response of scalp area involvement in the same patient following use of a phenol-acylated amino acid oil (Sarcophen). The oil was applied twice daily for a period of six weeks, resulting in almost complete disappearance of the persistent scaliness.

RESULTS OF TREATMENT WITH THREE NEW TOPICAL PREPARATIONS

ALTARA GELL		*ALTARA-CORT GELL*		*SARCOPHEN*	
PATIENTS	RESPONSE	PATIENTS	RESPONSE	PATIENTS	RESPONSE
13	21%++++	5	42%++++	18	37%++++
22	36%+++	3	25%+++	11	23%+++
14	23%++	2	17%++	10	21%++
7	11%+	1	8%+	7	14%+
5	9%°	1	8%°	3	5%°
61	100%	12	100%	49	100%

++++=Completely cleared; +++=Scales off, almost complete clearing; ++=Scales off, about half clearing; +=Improvement in scaling alone; °=No improvement.

acceptable to the patient, and since this results in negligent use poor therapeutic results are inevitable.

In the present series, patient cooperation was assured by the simplicity of application, acceptable cosmetic properties and non-staining quality of the preparations employed. Of the 74 patients studied, psoriasis was localized to the glabrous area in 61, to the intertriginous areas in 12, and to the scalp in 49. Trial in these patients showed that the allantoin-coal tar ointment was most effective in the glabrous areas, while optimal response in the patients with intertriginous involvement was produced by the allantoin-coal tar-hydrocortisone ointment. The oil containing phenol and an acylated amino acid in a non-aqueous menstruum was cosmetically acceptable to the 49 patients with psoriasis of the scalp, and proved uniformly effective in 39 (80%)

Summary

Three new topical preparations for treatment of psoriasis affecting specific areas of the body were used for 74 patients. Many of these patients had involvement of diverse areas, including the scalp. Of the 61 with psoriasis of the glabrous areas 49 (80%) experienced a satisfactory response to therapy with an allantoin-coal tar ointment. Of 12 patients with psoriasis of the intertriginous areas, 10 (83%) were materially benefited. Forty-nine of the patients were treated for psoriasis of the scalp with an oil containing phenol and an acylated amino acid, 39 (80%) exhibiting a satisfactory response. The total improvement rate with all three preparations was 80%.

Therapy of Skin Cancer

HERMANN PINKUS, M.D.,* *Detroit, Michigan*

►*Of the three most common types of skin carcinoma, basal-cell epithelioma and squamous-cell carcinoma are amenable to surgical or x-ray therapy, malignant melanoma to surgical therapy only. Proper treatment of all forms should result in a cure rate of close to 100 per cent. Suspected cases should be referred to specialists.*◄

Cancer of the skin, being accessible to inspection, palpation and any desired form of therapy, should have a cure rate of close to 100%. Statistics show only about 80% cures. A recent survey among dermatologists indicated 94% five-year cures.[1]

There are several reasons why cure is not achieved in every case of skin cancer. There are a few malignancies of such character that even earliest diagnosis and the most expert methods of treatment can not prevent a lethal outcome. In a much larger number of cases, failure can be traced to avoidable factors, especially delayed diagnosis and insufficient therapy. And in not a few cases treatment of skin tumors is overdone, because their nature is not clearly understood. While cure is achieved, the patient in such instances is exposed to unnecessary risk, disability and expense, and possibly is left with a greater cosmetic defect than is unavoidable.

* Chairman, Department of Dermatology Wayne State University College of Medicine.

1. Ferrara, R. J., *A.M.A. Arch. Dermat.*, In press.

Diagnosis

Every cancer of the skin is visible to the naked eye and accessible to the palpating finger. There are, however, many benign skin lesions, which look and feel very similar. Therefore, the patient often delays seeking medical advice, and the physician sometimes makes light of the patient's fears and advises no treatment, or he destroys a lesion without working out full diagnosis, only to see it recur and pose a bigger problem.

Due to years of public education, patients seek advice for many rather insignificant looking blemishes and small growths.

It is impractical to remove all "spots" that worried patients present. However, if the physician feels that he can not completely reassure the patient, he has the duty to follow one of three avenues open to him. He can remove the tumor surgically if it is small, take a biopsy if it is large, or refer the patient immediately to a specialist. There is no room in modern cancer therapy for destructive measures without previous diagnosis.

The now general rule that all tissues removed in hospitals must be submitted to the pathologist should as well apply to office surgery of skin tumors, with two possible exceptions: Common warts removed from children, and moles or skin tags removed from adults, especially ladies, for purely cosmetic reasons. Any mole, cyst, or tumor, however, that has grown recently, has changed color, bled, discharged or shown signs of inflammation does not fall into the cosmetic category. If the physician desires to remove a growth by desiccation or cautery, he may first slice off the protruding portion with a knife, then use the electric needle on the remainder. Thus material for biopsy is obtained that in most cases will enable the pathologist to make a diagnosis.

The three most common types of skin cancer are basal cell epithelioma (rodent ulcer), squamous cell carcinoma, and malignant melanoma. Each deserves individual consideration because of great differences of growth habits and prognosis.

Basal-Cell Epithelioma

The rodent ulcer of Jacob, now usually designated basal-cell carcinoma, is the commonest and the least dangerous type of cutaneous malignant growth. It occurs most frequently on the face and adjoining parts, rarely on any extremity and practically never on palm or sole. It grows slowly, and there are but few authenticated cases in which metastasis occurred. It may, however, ulcerate, destroy large portions of the soft tissues, and even grow into cartilage and bone. In early stages, in which cure is easily achieved, are deceptively inconspicuous. The patient often relates that he had a pimple, or a mole, for months and sometimes years, which became sore at times and healed again. In recent years, more and more patients come in with small brownish or translucent papules on the skin, which only a trained eye suspects to be early carcinoma. While most patients so afflicted are in the 6th decade, it is not uncommon to see patients in their 20's and 30's with early basal-cell epitheliomas. Large

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Bagnall, A. W. (Univ. British Columbia, Vancouver, B. C.): A.M.A. Clinical Meeting (Scientific Section, Exhibit No. 124), Minneapolis, Minnesota, Dec. 2-5, 1958.

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Scherbel, A. L.; Harrison, J. W., and Atdjian, Martin: **Cleveland Clin. Quart. *25:95, April, 1958.***

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Cramer, Quentin (Kansas City): **Missouri Med. *55:1203, Nov., 1958.***

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statistics even include teenagers.[2]

The treatment of basal-cell cancer is a local problem. The danger of distant metastasis can be discounted. It is for this reason that dermatopathologists begin to prefer the designation "basal-cell epithelioma" reserving the dread word carcinoma for the squamous-cell cancers. Treatment must be planned according to the size and location of the individual lesion. It must be thorough, but need not be radical. Many tumors are well defined and embedded in organized stroma which confines them into a single mass. Others grow in an infiltrating manner, and their extent is judged with difficulty.

While most lesions are equally responsive to surgery and x-ray therapy, special circumstances may make one method preferable. Small papular and nodular lesions are easily handled by complete excision extending into the subcutaneous fat and including ⅛ inch (3 mm.) of normal tissue on all sides.

The entire specimen should be submitted to the pathologist who should cut sections through the short diameter in order to assure completeness of the excision. If all went well the cancer is cured by the time the sutures are removed. If the pathologist's examination reveals tumor tissue in the line of excision, or indicates an unusual infiltrating type of growth, there is still time for re-excision or for x-ray therapy.

Lesions deemed too large for complete excision and suture should be biopsied in every case for definitive diagnosis. The patient then may be treated by excision and some form of plastic surgery to cover the defect, or it may be preferable to eradicate the tumor by x-ray treatment. This should be administered by a dermatologist or radiologist experienced in the treatment of skin cancer, using properly calibrated equipment. Haphazard application of an unknown dose from a diagnostic unit, as was done in times past, is worse than no treatment at all.

These principles cover the great majority of cases. However, three rarer types of basal-cell epithelioma need special mention. One is the sclerosing or morphea-type which grows slowly as an indurated plaque, often ulcerates only after many years. It is practically impossible to judge the extent of this type by inspection and palpation. Cords of tumor may extend for as much as an inch (2½ cm.) beyond the recognizable border. It also may invade subcutaneous

2. Pinkus, H., Symposium on Malignant and Premalignant Conditions of the Skin, in The Human Integument, American Association for Advancement of Science, 1959, pp. 193-212.

fat deeper than the most pessimistic estimate. These tumors are almost completely radioresistant. They require extensive surgery in close cooperation with a pathologist who must carefully examine all the borders of excised tissue. These cases often are best treated by the controlled chemosurgery of Mohs,[3] in centers where this method is available.

The second type is the dreaded "terebrans" form, the morphology of which differs in no way from run-of-the-mill basal-cell epithelioma. Yet it seems to be completely radioresistant from the beginning, and escapes routine surgical removal because it invades deeper tissues early. If an epithelioma recurs after what seems adequate irradiation or surgery, one should suspect something extraordinary, and resort to much more radical than routine surgery or to the chemosurgery of Mohs. These tumors may otherwise grow into muscle and bone, destroy the entire face and kill, even though they don't metastasize.

The third type is at the other end of the scale. Superficial basal-cell ("multicentric") epitheliomas remain restricted to the upper layers of the cutis for many years. They are more commonly encountered on the trunk, but may be found on face and scalp. Small lesions are inconspicuous flat papules or plaques, often mistaken for tinea, psoriasis, or eczema. They grow slowly as a thin plate in the skin and may reach the size of the palm. While the treatment of small lesions is easily accomplished by either excision or x-ray therapy, larger ones become a problem to the surgeon and the radiologist. Complete excision and skin graft may hospitalize the patient for some time, leave unsightly scars, and often is followed by recurrence in the periphery. Irradiation must be given in cancericidal doses over a rather large area and often leaves behind chronic x-ray sequelae cosmetically undesirable, and possibly lead to the dangerous squamous cell carcinoma. Here sharp curettage followed by electrofulguration of the base of the denuded area is the best therapy. Because the tumor tissue is well demarcated by stroma and inflammatory reaction, the curette removes exactly what needs to be removed, leaving behind the uninvolved part of the corium for quick closure of the wound by granulation. The hand of an experienced operator feels the borders of the involved tissues, and cure rate and cosmetic results are satisfactory. This form of therapy should be used only after histologic diagnosis is e

3. Mohs, F. E., Chemosurgery in Cancer, Gangrene and Infection, C. C. Thomas, Springfield, Ill., 1956.

tablished, and by a well trained dermatologist.

Squamous-Cell Carcinoma

This carcinoma, somewhat less common, but much more dangerous than, basal-cell epithelioma, affects mainly the exposed areas of the skin, face, neck, and hands. The lower lip of men is a preferred site. Lesions in this location share with those of the glans penis, vulva, and anus the tendency to metastasize much more readily than cancers of the skin proper. There is often a precursor stage, most commonly the so-called keratosis senilis, actually a form of sun-ray damage of the skin. Keratoses and the cancers which develop in them therefore are more commonly found in farmers and other persons following outdoor occupations, and are much more frequent in southern U.S. than in less sunny areas. The fair, freckling skin is the type most often involved. Ultraviolet rays of the sun play here a carcinogenic role similar to that of x-rays, tar, and arsenic in a smaller number of cases.

Clinical differentiation of squamous-cell from the less-malignant basal cell epithelioma, from not-yet-invasive solar keratoses, and from innocent seborrheic keratoses and warts is difficult. Therefore, the previously mentioned rule should apply that none of these lesions should be destroyed or removed without pathologic examination. Tissue obtained by slicing off the superficial portion is usually sufficient for histologic diagnosis, or a small biopsy may be taken. Obtaining it need not delay or complicate any form of intended therapy.

Most lesions, if caught early, are just as curable by x-radiation as by surgery. Notable exceptions are carcinomas of the dorsum of the hand, where surgery is preferable because adequate x-ray dosage may lead to ulceration and possible sloughing of tendons. Divided and protracted x-ray schedules can be applied to lesions on nose and ear without excessive damage to cartilage, often with excellent cosmetic results, where surgery would have been mutilating. Excision must be wider than in basal-cell epithelioma. Any patient having squamous-cell carcinoma must be examined carefully for evidence of metastasis to draining lymph nodes. While prophylactic resection of nodes is not indicated, any enlarged node should be investigated.

A surprising development of recent years is the realization that there are self-healing squamous-cell cancers of the skin. Two main types are recognized: the multiple lesions of Ferguson Smith and the single molluscum

sebaceum, or kerato-acanthoma. The tumor-like keratoses of Poth are related to the latter. Ferguson Smith reported that some patients repeatedly develop tumors which are indistinguishable clinically or microscopically from squamous-cell carcinoma, but grow for a time, then stop, dry up and heal without therapy. This experience is rare, but the single lesion, the kerato-acanthoma, is common. These tumors grow quite rapidly and reach a size of ½ inch (1-2 cm.) or more in a few weeks or months. They usually have a volcano-like appearance—slopes covered with smooth-stretched skin and a central crater filled with a tough and adherent keratotic plug. If the patient delays seeing a doctor or if the physician has the courage to wait, growth ceases after three to six months; the mass becomes sequestered by inflammatory reaction, and the tumor heals, leaving a depressed, irregular scar. Simple excision or moderate doses of x-ray lead to permanent cure; even curettage and cautery are sufficient.

When these lesions come to the pathologist there is a certain paradox. In spite of their rapid growth, they consist of fairly well differentiated prickle cells, with a strong tendency to keratinization. In some cases the picture is that of pseudo-epitheliomatous proliferation, but in others it cannot be distinguished from true carcinoma of low grade (Broders' grade I). The pathologist must admit his inability to make a definitive diagnosis of kerato-acanthoma on histologic grounds alone and turn the responsibility over to the clinician who must decide on the basis of clinical features, namely, rapidity of growth in the face of well-differentiated, low-grade histologic characteristics. The responsibility of both, clinician and pathologist, is great in these cases. However, unnecessarily extensive operations, even amputations, may be avoided by recognizing this new entity of kerato-acanthoma.

Malignant Melanoma

The treatment of malignant melanoma is entirely surgical although recent European publications have claimed a place for high doses of contact x-ray therapy. This is at best a highly specialized procedure. Surgery must be radical, and preferably prophylactic.

The question of the pigmented mole developing into malignant melanoma—either spontaneously or following traumatization by accident and especially, by injudicious treatment—has provoked much heat. There is little doubt that a considerable percentage of malignant melanoma develop in a pre-existent benign

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mole. Conversely, in view of the great frequency of benign moles, it is a rare occurrence for a pigmented nevus to develop into malignant melanoma. There is little evidence that single trauma can convert a benign mole into melanoma. Some experts contend that any melanoma which seems to follow slight trauma was pre-existent.[4]

This, however, affords little consolation to the physician who has desiccated a supposedly benign nevus and then finds the patient developing a malignant recrudescence or distant metastasis. He cannot prove that the "mole" was cancer before he ever touched it. Several published statistics,[5,6] and my own experience, indicate that the incidence of disagreement between clinical and histologic diagnosis is high in the field of pigmented lesions. The only insurance against error, blame, and possible serious consequences for patient and doctor, is histologic examination on every mole removed, unless removal is practiced for strictly cosmetic purposes. This, of course, precludes simple desiccation as a method of treatment. However, superficial ablation of the protruding portion of a nevus, followed by desiccation, does not increase the amount of scarring and furnishes a satisfactory specimen, since malignant change always starts at the dermo-epidermal junction.[7]

A junction nevus in a child need not cause concern, unless there is other evidence of malignancy. Malignant melanoma is rare in children. We have learned, though, that many lesions formerly diagnosed as malignant constitute a special type of tumor, the juvenile melanoma.[8] These lesions look frightening under the microscope to one not familiar with them. They do not recur or metastasize if removed completely, though conservatively, during childhood.

A word may be said concerning the handling of a mole that is suspected to be malignant. If at all possible (if the lesion is not too large), conservative but complete excision is preferable to removal of a piece. If histologic examination proves the lesion to be benign, nothing more need be done. If it is malignant the patient's chances have not been jeopardized by the first procedure.

Conclusions

In the tumor conferences of large hospitals, surgeons and radiologists usually contend for the treatment of skin cancer pa

4. Pinkus, H., *J. Michigan M. Soc.*, 58:576-580,1959.
5. Becker, S. W., *Arch. Dermat. & Syph.*, 60: 44-65,1949.
6. McMullan, F. H., & Hubener, L. F., *A.M.A. Arch. Dermat.*, 74:618-619,1956.
7. Shaffer, B., *J.A.M.A.*, 161:1222-1226,19
8. Spitz, S., *Am. J. Path.*, 24:591-610,194

tients. Only too often, the dermatologist and the general practitioner are blamed for their initial handling of cases now far advanced. While in a number of cases this blame is justified, tumor boards are apt to forget that they see only the few cases not cured in the practitioner's office. Yet a cure rate of 80% certainly is capable of being improved. The foregoing discussion is a practicing dermatologist's opinion of how this can be done in the general practitioner's office who possibly does not have ready access to specialistic consultation. A high index of suspicion and avoidance of the attitude that treats almost any skin lesion as a minor matter will improve cure rate. It has also been pointed out how over-treatment should be avoided in certain cases.

Summary

The cure rate of skin cancer can be improved by early and rational therapy based on accurate diagnosis. The more common forms, basal-cell epithelioma and squamous-cell carcinoma, are usually amenable to surgery or x-ray treatment. Every case, however, should be weighed individually in order to achieve cure with a minimum of morbidity and disfigurement. Malignant melanoma is entirely a surgical problem, in which increased emphasis should be placed on prophylaxis.◀

Present Evaluation of Chlorpromazine

A continued survey for four years was made of once nudistic, incontinent, combative, destructive patients, the majority hospitalized to 15 years, who were treated with chlorpromazine. Of 822 patients treated, 258 were discharged and 77 (29.8%) returned. Only 26 of the 77 returnees represent relapses while taking the drug diligently. Fifty-five of the 181 patients remaining outside the institution have found gainful employment.

Placebos were given to 72 discharged patients, 43 of whom relapsed, indicating that the patient having had lengthy hospitalization and having been severely regressed prior to treatment, may need drug treatment for an indefinite time. Six of the patients have been away from the institution for 3½ years, 36 for more than three years. Chlorpromazine represents an indispensable mode of treatment in the highly regressed patient recently discharged after prolonged hospitalization.

Tuteur, W., et al., *Illinois M.J.*, 116:9-12, 1959.

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Therapy of Anemia in Pregnancy

WILLIAM M. CENTER, M.D., *San Antonio, Texas*

►*Of 18 pregnant women treated for associated anemias and given red cell count, hemoglobin level and hematocrit readings two weeks before delivery, all of 10 receiving a cobalt chloride-ferrous sulfate combination showed significant increases for each of the readings, indicating a more useful therapeutic adjunct.*◄

Pregnancy constitutes one of the major physiologic demands for iron and frequently gives rise to a state of serious iron want. Although pregnancy anemia usually is seen only during the later stages of gestation, recent studies have shown that a slight but definite anemia may be demonstrated even in the first trimester.[1] This anemia has none of the characteristics of iron deficiency. If the fetal demand can be compensated by increased absorption and by the conservation of iron due to the cessation of menstruation, the anemia does not progress. However, this is not usually the case.

In the last trimester of pregnancy, the rapidly growing fetus requires approximately 4 mg. of iron per day, a total of about 300 mg.[1] At the same time, the maternal hemoglobin mass increases to a degree calling for an additional 500 mg. of iron.[2] The combination of the iron contained in the mother's increased hemoglobin mass and that required by the fetus exceeds by more than 200 mg. the amount conserved through the cessation of menstruation.[3] Storage iron can be utilized to satisfy the demands of pregnancy, but a majority of women have reduced iron stores at the beginning of gestation.[4] As pregnancy advances, therefore, anemia becomes more pronounced and features of iron deficiency become evident.[5,6]

Daily oral supplements of ferrous sulfate begun during the

1. Sturgeon, P., *Pediatrics*, 18:267,1956.
2. Pribilla, W., et al., Iron in Clinical Medicine, University of California Press, 1958, pp. 58-64.
3. Moore, C. V., *Am. J. Clin. Nutrition*, 3:1, 1955.
4. Holly, R. G., & Grund, W. Y., *Am. J. Obst. & Gynec.*, 77:731,1959.
5. Holly, R. G., *Clin. Obst. & Gynec.*, 1:15, 1958.
6. Sturgeon, P., *Brit. J. Hematol.*, 5:31,1959.

first trimester will frequently check the progress of the anemia of pregnancy and reduce or eliminate the manifestations of iron deficiency. For this reason, dietary iron supplementation has come to be widely used as a part of routine prenatal care in this country. Statistical evidence has been presented that significantly better clinical results can be obtained if cobalt is given with iron for the treatment and prevention of pregnancy anemia.[7-9] To date, however, this work[7-9] has provided the only published reports giving a detailed comparison of the results obtained with iron alone as against combined cobalt-iron therapy in parallel series of patients.

Material and Methods of Study

The subjects of this study were unselected pregnant women at a Salvation Army Home and Hospital. The age range was from 14 to 38 years. These women were under close supervision throughout the course of the investigation. They were domiciled where a registered nurse was in constant attendance. Their diet and medication were rigorously controlled at all times. They were admitted several months prior to delivery and all but one remained for six weeks thereafter.

At the time of admission, a complete history and a blood specimen for careful examination was obtained from each patient. The week of gestation average was 20 ± 2.8 weeks. Hemoglobin concentrations were determined by the alkaline hematin method[10] using a photocolorimeter calibrated by the oxygen capacity method.[11] Red and white cell counts were made in routine fashion with a hemacytometer. The hematocrit was determined by the Wintrobe technique,[12] the hemotologic determinations all done by one registered technician. Bone marrow specimens were obtained from five patients at the time of admission; four consented to the taking of a second specimen two weeks before delivery. These specimens were stained for iron with prussian blue and were examined by a pathologist.

Eight patients were given tablets containing 200 mg. of exsiccated ferrous sulfate while 10 received enteric coated tablets each containing 15 mg. of cobalt chloride and 100 mg. of exsiccated ferrous sulfate.* The dosage in every case was one tablet four times daily with meals and at bedtime. Therapy was begun im-

7. Holly, R. G., *Obst. & Gynec.*, 9:299,1957.
8. Holly, R. G., *Obst. & Gynec.*, 5:1,1955.
9. Hamilton, H. G., *South. M.J.*, 49:1056, 1956.

*Roncovite-MF®, Lloyd Brothers, Inc., Cincinnati.

10. Clegg, J. W., & King, E. T., *Brit. M.J.*, 1: 329,1942.
11. Wintrobe, M. M., Clinical Hematology, Fourth Edition, Lea & Febiger, Philadelphia, 1956, p. 385.
12. Wintrobe, M. M., *J. Lab. & Clin. Med.*, 15:287,1929.

mediately upon admission and continued for one or two weeks after delivery, the period of treatment 11 to 26 weeks.

Results

The subjects of this study were generally "run down" at the time of admission. The initial hematologic findings showed that all of the women had low blood hemoglobin concentrations, ranging from 7.0 to 10.4 gm./100 cc., average 8.76±1.01. The hematocrit values were also uniformly low, 21 to 38% (average 30 ± 4.5), and the red cell count range was 2.74 to 3.63 million per cm., average 3.22 ± 0.29.

In 13 patients the anemia was hypochromic, mean corpuscular hemoglobin concentrations 21 to 31%, average 27 ± 3.0, instead of the normal 34±2%. The remaining five patients had M.C.H.C. values within the normal range. In two cases the anemia was microcytic—corpuscular volume 70 to 73 cu. micra, nine patients showed macrocytosis—M.C.V.>92 cu. micra, while seven had M.C.V. values in the normal range. The bone marrow smears of the five patients who submitted to sternal puncture gave negligible or no evidence of iron deposits.

When re-examined two weeks prior to the expected date of delivery, all of the women who were given Roncovite-MF showed increases in their blood hemoglobin concentrations, range 0.4 to 2.7 gm./100 cc. (aver. 1.62 ± 0.75), this accompanied in every case by an increase in the red cell count of 300 to 960 thousand per cu. mm. In two patients the hematocrit was restored to the normal range; all showed improvement in the readings. Three who were given Roncovite-MF consented again to having bone marrow biopsy specimens taken about two weeks before they were expected to deliver, two smears showing a definite increase of iron-staining (prussian blue) material, the third a questionable increase.

In the group of eight women who received ferrous sulfate, 200 mg., q.i.d., only four showed increased hemoglobin when examined two weeks prior to delivery. The increases ranged from 0.75 to 2.45 gm./100 cc., average 1.45 ± 0.50. There were parallel increases in these patients' red cell counts of 50 to 680 thousand per cu. mm., average 410 thousand. A slight decrease occurred in the red cell count of one of the women, who likewise showed a slight decrease in blood hemoglobin concentration. T e hematocrit was increased in all but this one patient, but in only one was the value restored to the normal.

In the group receiving ferrous sulfate, 800 mg. per day, the

women had been treated for periods ranging from 11 to 23 weeks. No reason was found for the failure in three patients.

Of the ten patients who were given Roncovite-MF, eight responded with hemoglobin increases of 1.35 to 5.15 gm./100 cc. There was no apparent reason for the poor results in two cases.

Discussion

It has long been recognized that iron demands are increased in pregnancy because of the requirements of the fetus, and it has repeatedly been shown that many healthy women lack iron reserves adequate to meet these requirements and still maintain their circulating hemoglobin mass in the normal range. Thus, in a group of women who received no supplemental iron during pregnancy, two-thirds had hemoglobin concentration below 12 gm./100 cc., of blood two weeks prior to delivery.[7] In a similar group of women given supplemental iron, 80 per cent had blood hemoglobin concentrations above 12 gm./100 cc. two weeks before delivery. What does not appear to be generally understood is that better results can be obtained in the treatment and prevention of pregnancy anemia by giving cobalt with iron. In a group of patients receiving iron and cobalt 90 per cent maintained hemoglobin concentrations above 12 gm./100 cc. to delivery, two-thirds a leve above 13 gm./100 cc.[7]

Our own results in this care fully controlled series are in com plete agreement with these[7] find ings. In the group receiving fe rous sulfate, 200 mg. q.i.d., fiv of the eight patients responde with a significant improvement i their circulating hemoglobin mas The average increase amounte to about 3.0 gm./100 cc. If, hov ever, we accept 12 gm./100 c as the lower limit of "normal" f the blood hemoglobin concentr tion in pregnant women, a s isfactory therapeutic result w not achieved in any of these p tients. By way of contrast all b two of the patients given cob and iron showed appreciable i creases in their hemoglobin co centrations, and two of them tained "normal" values for t index. This superior result w achieved, moreover, with o half the daily dosage of i given to the patients who w treated with ferrous sulfa alone. Thus, utilization of ora administered iron was increa roughly two-fold by the sim taneous administration of cob

The reasons for the inadequ response in five of our patie are not definitely known. So recent findings appear to of an explanation.[7] Iron utilizat was studied in four pregna women who were given injecti

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of the iron isotope, Fe^{59}, intravenously. Evidence was obtained that at least in some pregnant women iron utilization is poor, possibly due to bone marrow depression. This would also help to explain the significantly better clinical response of the group receiving cobalt and iron, since cobalt stimulates the bone marrow by virtue of its action in enhancing the production of erythropoietin, the erythropoietic hormone.[13]

Summary

A comparison was made of the results of therapy with iron alone, and with cobalt and iron, in 18 institutionalized pregnant women, all anemic at the time treatment was begun between the 14th and 24th weeks of gestation. Bone marrow smears stained with prussian blue revealed negligible or no evidence of iron deposits (hemosiderin). When examined two weeks prior to delivery, all 10 women taking cobalt and iron were found to have increased red cell counts, hemoglobin levels and hematocrit readings. The average increase in hemoglobin concentration amounted to 1.62 gm./100 cc. Of the three who consented to having bone marrow biopsies repeated, two had definitely increased deposits of marrow iron, the third a questionable increase.

All but one of the eight women taking ferrous sulfate, 200 mg. q.i.d., had increased hematocrit readings, only four showed increased red blood cells and hemoglobin two weeks before delivery. No significant increase in iron-stainable material was seen in the bone marrow smears of the one patient in this group who again consented to having a marrow specimen taken.

Since the women taking ferrous sulfate tablets received twice as much iron as those treated with the cobalt and iron preparation, it appears that in the latter group the absorption and utilization of orally administered iron was approximately doubled by concomitant administration of cobalt.

The data of this controlled study tends to illustrate the superiority of cobalt-iron therapy over treatment with iron alone not only for the correction of anemia, but also for repletion of iron stores in pregnant women.

13. Goldwasser, E., et al., *Science*, 125:1085, 1957.

Ano-Rectal Disease: Office Diagnosis and Treatment

WALTER H. HAMILTON, M.D., EDWIN B. HAMILTON, M.D., and CHARLES H. HAMILTON, M.D., *Columbus, Ohio*

The methods and techniques described for the treatment of ano-rectal disorders are only applicable following correct diagnosis, this usually accomplished satisfactorily by the general practitioner in the office with the aid of the examining finger and proctoscope. Early, correct diagnosis will aid treatment by the specialist.

The family physician is capable of diagnosing practically all proctologic disease conditions. He may then either treat the patient himself or refer to a specialist.

Diagnosis

With an examining finger and proctoscope more than 75 per cent of cases of ano-rectal disease can be correctly diagnosed. The three most common symptoms are bleeding, pain and itching. Rectal bleeding should never be lightly dismissed as due to "a slight case of hemorrhoids." Bleeding with prolapse of tissue from the anus is most likely due to hemorrhoids. Slight bleeding plus pain with defecation, followed by burning, is probably caused by a fissure or cryptitis. Bloody diarrhea of a chronic type, with or without lower abdominal cramping or deep pelvic pressure discomfort, may be due to ulcerative proctocolitis or to rectal carcinoma. Painless rectal bleeding may occur with a polyp in the rectum or with ulceration of internal hemorrhoids.

Pain is perhaps the most important symptom in the patient's mind, for which reason the physician should be gentle during diagnostic or treatment procedures. Efforts toward this end will be appreciated by these patients. Knowledge of the location, duration and nature of the patient's pain will help to make the diagnosis. The pain of a perianal or perirectal abscess comes on gradually and is diffuse, persistent and aching. The patient

will usually report the presence of a tender lump or indurated area.

The pain of an anal fissure (ulcer) is severe, sharp and penetrating. It reaches its peak with passage of stool over the raw defect in the anal lining. There is usually residual burning pain for several hours following defecation. The vast majority of anal ulcers occur in the posterior mid-line. The patient will not infrequently be able to localize his discomfort to that point. The pain of hemorrhoids with prolapse may be dull, aching, burning or sharp. It is usually worse during or after defecation. Some relief may be obtained by manually replacing the prolapsed tissue. The pain of an acute thrombotic external hemorrhoid is intense, usually comes on rapidly following straining at stool. There is an extremely tender mass (or masses) in the perianal skin. Not uncommonly the patient will try to replace this mass up through the anus, without success.

In case of itching about the ano-rectal region, fistula-in-ano with associated perianal drainage, pinworms, pruritus, cryptitis and drug-induced dermatitides must all be considered. The pertinent history together with adequate physical examination will usually demonstrate the cause.

Physical Examination

Adequate examination for proctologic disease consists of external inspection of the buttocks and perianal region, palpation of the perianal, anal and rectal anatomy and endoscopic viewing of the anal canal and rectal ampulla. The patient in the Sims position and the examiner on a stool of appropriate height are best positions. With the buttocks spread, inspection is made for abnormalities of the perianal skin, sinus openings, signs of inflammation and discharges. Next the perianal area is palpated, this followed by careful examination of the entire circumference of the anal canal and lower ampulla. Abnormalities of coccyx, prostate gland and uterus may be noted, and any abnormal exudate or discharge, as well as the color of stool on the glove. Soft polyps and internal hemorrhoids are difficult to diagnose by palpation. In contrast, 50 per cent of rectal cancers can be felt through the anus. Typically the lesion is hard or gristly about its margins and ulcerated in the center.

It should not be necessary to mention the importance of gentleness during examination. The examining finger should in every instance be well lubricated and tender areas should be avoided if possible without sacrificing

completeness of examination. It is well to remember that rectal abnormalities may be palpated transvaginally in the female thus avoiding painful anal lesions. If patients whose symptoms are extremely acute at the time of initial examination (such as is found in acute fissure, inflammatory stricture or thrombotic hemorrhoids), it may be discreet to omit parts of the examination until a later visit. In the interim treatment should be directed toward reducing the acuteness of the symptoms with conservative means, such as moist heat and appropriate analgesics. However, if it seems mandatory to insert a finger or an instrument into the spastic anal canal, application of the topical anesthetic pramoxine HCl is judicious. This medication, unlike many of the other topical anesthetics, rarely causes a sensitivity reaction.

Much is Revealed by Having the Patient "Strain Down"

Following inspection and digital examination, have the patient strain down to demonstrate presence and degree of hemorrhoidal prolapse. In the case of combined (internal and external) hemorrhoids the contrast is marked, since the external plexus is covered by skin and the internal by pink-red mucosa. A thrombotic external hemorrhoid is blue-black beneath the perianal skin and is exquisitely tender to touch. An abscess usually shows signs of inflammation and is not difficult to differentiate from a thrombus. Palpable induration in the perianal area with an associated sinus opening, perhaps with expressible exudate, indicates a fistula-in-ano. Chronic pruritus is commonly accompanied by thickening of the perianal skin, multiple fissures or abrasions.

Endoscopic Examination

The knee-chest or inverted position using the tilt table is preferred for this procedure. It permits the colon to fall upward and forward thus facilitating passage of the sigmoidoscope. In addition to the basic equipment a long metal suction tube and a supply of long cotton swabs are at hand. A repeat digital examination should precede insertion of the instrument. Then the well-lubricated scope with obturator in place is gently passed through into the lower rectum, the obturator removed and replaced with the light carrier.

The remainder of the examination is completed under constant visualization and the basic tenet of never blindly forcing the instrument is followed. The scope is passed up the lumen of the bowel gradually. It may have to be withdrawn a few centimeters at times to assure safe pas-

sage past the valves and redundant mucosal folds. It may be necessary to use the bellows attachment to slightly balloon out the bowel. The patient should be forewarned that he may feel some cramping and fullness as the scope is passed beyond the 15-cm. mark, especially if the bellows is being used.

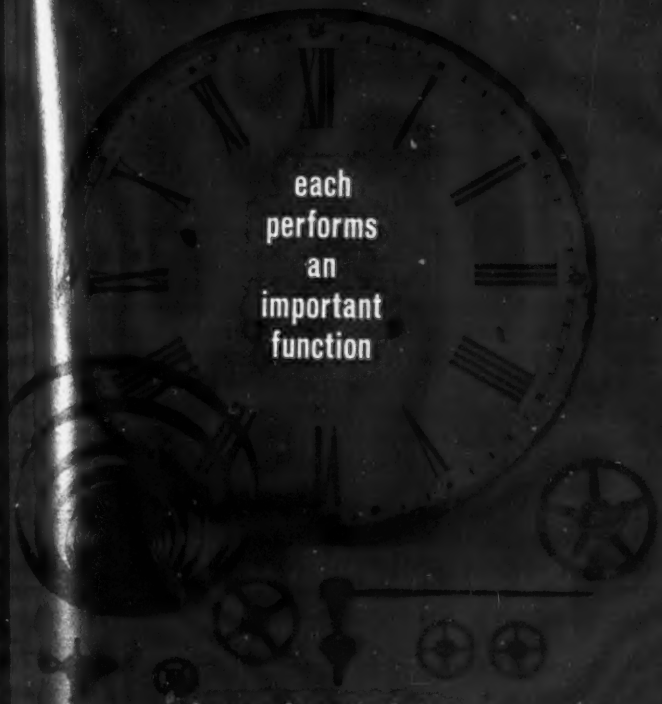
A small dose of an analgesic may be administered prior to sigmoidoscopy in the unusually sensitive or apprehensive patient. Abnormalities are best visualized as the scope is withdrawn. A gentle circular motion is used as the instrument is slowly withdrawn in order to visualize the entire mucosal surface. The suction tube and cotton swabs should be used freely to clear away liquid and solid matter which may obscure the view. Sometimes the scope cannot be passed its full length. It should not be forced. A barium enema may be necessary.

Adenomas (polyps) usually will bleed when wiped with a swab. A localized area of bleeding and ulceration with an ill-smelling discharge is typical of adenocarcinoma. Diffuse granularity and many small areas of ulceration which bleed easily indicate ulcerative proctitis, or colitis. Larger ulcerations with broad intervening areas of normal-appearing mucosa are likely due to amebiasis and may be diagnosed by sending a suspension of saline irrigant to the nearest reliable laboratory.

Disease of the lower rectum and anal canal may be better visualized with an anoscope. We prefer the Brinkerhof type which has an easily removed sliding segment. Thus each quadrant of the canal may be visualized. Internal hemorrhoids may be easily seen just above the dentate line as they prolapse into the lumen. The anal crypts should be thoroughly investigated for inflammation, ulceration or bleeding. Hypertrophied papillae are indicative of chronic inflammatory disease. Gentle use of an anal crypt hook may reveal a deep crypt or the origin of a fistula-in-ano. Particular attention should be directed toward the posterior mid-line for the majority of anal fissures occur there.

Office Treatment

Pruritis ani can practically always be managed in the office. We prefer to omit topical anesthetic ointments because of the high incidence of skin sensitization. Instead we use frequent applications of mild astringents (boric acid or witch hazel), oral sedation, omission of soap in the perianal area, and use of moistened cotton to cleanse following defecation. These patients must be informed that the response



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treatment will be slow.

Thrombotic external hemorrhoids may be safely treated in the office if the involvement is not too extensive. Cases of thrombosis in the external plexus must be differentiated from those in which there is a combined hemorrhoid with external thrombosis fed by an active pedicle artery. The latter type is prone to bleed following enucleation of the thrombus.

Generally injection of the perianal skin over and distal to the thrombus with procaine (1%) using a 26-gauge needle gives adequate anesthesia and the skin and thrombus may be excised without difficulty. A pressure dressing should be applied and sitz baths withheld for eight hours.

Small abscesses about the anus may be incised and drained in the office; 2% lidocaine is excellent for local anesthesia in such cases. Large abscesses should be treated in hospital under regional or general anesthesia where extensive drainage can be attained.

Most acute anal fissures may be treated in the office with satisfactory results. These lesions should never be cauterized with silver nitrate. Frequent sitz baths, adequate water intake and prevention of constipation or diarrhea permit healing to progress.

Injection of a single, well localized bleeding internal hemorrhoid may be performed in the office. Large multiple internal hemorrhoids or low-lying hemorrhoids which are in the somatic nerve zone should never be sclerosed. We prefer quinine and urea HCl (5%) and inject a very small quantity using a long flexible or angulated needle (22- to 25-gauge). One-fifth to two-fifths of a cc. is deposited at the superior aspect of the lesion into the submucosa (*not* into the vein). It is usually necessary to inject the hemorrhoid at weekly intervals, for three or four weeks.

Biopsy of rectal tumors through a proctoscope may be performed in the office with relative safety. It is usually not necessary to cauterize biopsy sites, but in removing small adenomatous polyps the base may be electrocauterized.

Lesions which should be treated in hospital:

1. Prolapsing hemorrhoids or hemorrhoids with extensive thrombosis.

2. Chronic anal fissures (ulcers) and fistulae-in-ano.

3. Large ischio-rectal or perirectal abcesses.

4. Adenomatous polyps greater than 1.5 cm. in diameter, especially if located in the upper rectum or above the peritoneal reflection.

5. Carcinoma of the anus or rectum.

Summary

Proctologic disease is common and more physicians should feel capable of diagnosing and treating these ailments.

One-half of all cancers of the colon and rectum may be felt with the examining finger. The physician in general practice has the best opportunity to diagnose cancer in this region early and reduce the period of delay between diagnosis and curative treatment.◀

Decubitus Ulcers: Promotion of Healing with Sheepskins

Local treatment of an ulcer should be to assure optimum availability of reduced physiologic defense forces at the site. Ointments and proteolytic enzymes are not indicated. Thorough debridement by sharp dissection is time-saving and a certain way of cleaning an old ulcer.

A preventive appliance of sheepskins must be large enough to cover all bony surfaces, and the heels, elbows, and the occiput if the patient is helpless. Whenever a patient has possibilities of developing bed sores, he should immediately be placed on a sheepskin. If one skin is not large enough to cover all parts, two are used.

Debridement is made by sharp dissection and the patient placed on the sheepskin without dressings. The sheepskin is resilient, airy, does not wrinkle, permits even pressure over a large area with no rubbing or sliding, and absorbs and dissipates due to its spongy and airy qualities. The skin is changed when soiled (usually every three to seven days) and cleaned with mild soapy water or by spraying with a garden hose. It is then allowed to dry in open air and fluffed to its original state with a small brush.

An apoplectic, bedridden for three years and nursed at home without benefit of retention catheter, used up two skins in three years. Several large ulcers have healed completely in this patient. One, having exposed the sacrum, healed in 20 days.

In open treatment of burns of the chest and back patients are comfortable while reclining on a sheepskin, and when they turn in bed the skin doesn't stick. The device is also very efficacious as a bed covering for premature babies.

Davis, L., Jr., *J.M.A. Alabama*, 29:164-165, 1959.

A Modern Treatment of Seborrheic Dermatitis

S. M. PERLSTEIN, M.D.,* *Philadelphia, Pennsylvania*

►*Of 208 successive cases of seborrheic dermatitis, 96% were successfully treated with a shampoo containing a combination of surface cleansers and antiseptics. This preparation gained patient acceptance, needed no special rinses, and did not cause discoloration, irritation nor contact dermatitis.*◄

Seborrheic dermatitis is one of the most common eruptions seen in medical practice today. No infectious agent has been isolated despite the fact that some observers report transmission of the eruption from person to person.

The sites of predilection are the scalp, corona, pre- and postauricular areas, external ear canals, eyebrows, eyelids, alae nasi, umbilicus, presternal, interscapular and intertriginous regions. Overtreatment will precipitate an exfoliative dermatitis. The relationship of seborrheic dermatitis to blepharitis and the need for scalp therapy has been the subject of a recent report.[1]

A therapeutic shampoo† containing a combination of anionic surface cleansers and wetting agents (sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate), plus 2% sulfur, 2% salicylic acid, 1% hexachlorophene and kerohydric (a crystal clear dewaxed fraction of lanolin) to prevent excessive drying after shampooing is the subject of this report.

This preparation has many advantages:

1. Cosmetically appealing smooth lotion-like texture, appealing color and fragrance and abundant lather.
2. No need for additional soaps or detergents.
3. No metallic materials to produce alopecia.
4. No discoloration of hair.
5. No accidental conjunctivitis.

*Assistant Professor of Dermatology, Temple Medical Center.

†*Sebulex*®, Westwood Pharmaceuticals, Buffalo, N. Y.

1. Jordan, J. S., *Pennsylvania M.J.*, 62:712, 1959.

6. No increased sebum formation.

7. No primary irritancy or acute contact dermatitis.

8. It is inexpensive.

Study

In this series, 214 successive cases of seborrheic dermatitis were treated. Six cases could not be followed and were removed statistically. Excellent results were obtained in 200 of 208 patients (a 96% effective control rate). Two cases of psoriasis and one case of cradle cap were also successfully treated. Only one case preferred the cream form* of this preparation.[2-6] No cases of either primary irritancy or acute contact dermatitis were observed. Included were 138 females and 76 males, ranging from 14 to 65 years of age. Of these, 125 had seborrheic oleosa and 89 seborrheic sicca.

All patients were instructed to use the therapeutic shampoo twice a week for a period of two weeks, then once a week, or biweekly, as required. Scalp therapy is essential for the successful control of this eruption.

Summary

Of 208 successive cases of seborrheic dermatitis, 96 per cent were successfully treated with the new antiseborrheic shampoo. No cases of primary irritancy or acute contact dermatitis were observed.◀

*Fostex Cream®, Westwood Pharmaceuticals, Buffalo, N. Y.

2. Robinson, A. M., *J. South Carolina M.A.*, 52:253,1952.
3. Finnerty, E. F., Jr., *New England J. Med.*, 255:614,1956.
4. Howell, C. M., Jr., *Am. Pract.*, 8:223,1957.
5. Edelstein, A. J., *Pennsylvania M.J.*, 6 851,1957.
6. Perlstein, S. M., *Pennsylvania M.J.*, 6 218,1958.

Deepening of the Voice in Pregnancy

Deepening of the voice occurs in about one pregnant woman in every 5 as a result of laryngopathia gravidarum. This feature of toxemia of pregnancy is caused by vasomotor and secretory disturbances of the upper respiratory mucosa. Usually the voice returns to normal soon after parturition. In an illustrative case, change to a manlike voice has continued for 9 years. The change of voice occurred together with enlargement of the larynx in the patient's second pregnancy. A third pregnancy did not affect the condition. Although there may be some endocrine dysfunction in this woman, no other symptoms of such a disorder have been found.

Nessel, E., *München. med. Wchnschr.*, 1007,1959.

Clinical and Metabolic Effects of Hydrochlorothiazide

VICTOR VERTES, M.D.,* *Cleveland, Ohio*

►*A study of the clinical and metabolic effects of hydrochlorothiazide indicates its effectiveness in the treatment of edematous states due to sodium retention and also (in conjunction with a "priming" low-salt diet) in the treatment of hypertension. This agent should be used cautiously in treating renal disease.*◄

The chlorothiazide group of drugs are potent diuretic agents and, in a good number of cases, have a marked antihypertensive effect. Hydrochlorothiazide differs from chlorothiazide in that the heterocyclic ring of the compound is completely saturated. This change in the chemical structure of the drug increases its potency ten times. The mode of action of both these drugs is the same and the advantage of the use of hydrochlorothiazide is that smaller doses are required for clinical effects. This might result in fewer side reactions.

*Director Endocrine and Metabolic Laboratory, Division of Medicine, Mount Sinai Hospital, Cleveland, Ohio.

Method of Study

In order to define the sodium, chloride, potassium, and water diuretic effects of hydrochlorothiazide, patients with hypertension, edema, or both, were admitted in the Metabolic Ward of the hospital. The hypertensive group of patients had been followed for at least one month in the Out-Patient Department and had been on no drug therapy for their hypertension during this period. The patients with edema were admitted and baseline stable weights on a low-salt (1 gram) diet were obtained. Upon admission to the ward the hypertensive group was also given a 1 gram salt diet. Following an adequate baseline period, the patients were treated with hydrochlorothiazide, 50 mg. three times a day, and the low-salt diet was continued. After one week of observation the patients were discharged to be followed at two-week intervals in the Out-

Patient Department. The low-salt diet was discontinued and the patients had no restriction of their sodium intake and had only to take 50 mg. of hydrochlorothiazide, three times a day. Throughout the study period in the hospital and during the Out-Patient Department follow-up, serum electrolytes and 24-hour urinary excretions of electrolytes were determined. Blood pressures and weights were recorded throughout the study.

Results

Most of the patients with hypertension had a slight drop in their blood pressure while on the low-sodium diet. When hydrochlorothiazide was added, a further significant lowering occurred and reached normotensive levels in the majority of cases. Initially the patients experienced a Na, Cl, and H_2O diuresis along with a slight increase in K excretion. This increased water and electrolyte loss decreased as the low-salt diet was continued. After discharge from the hospital and a return to a general diet, the electrolyte excretion again increased to levels above those obtained during the baseline period. The blood pressure remained down in these patients even though they were not on a limited diet. During the course of follow-up, several patients "escaped" from therapy and their blood pressures tended to rise. A return to a low-sodium diet, plus the continuation of hydroclorothiazide, again produced lowering of pressure in these patients.

The patients with edema also had a Na, Cl, K, and H_2O diuresis with hydrochlorothiazide. In patients with large amounts of edema fluid, the diuresis continued throughout the time they were on a low-salt diet. Those patients who reached "dry weight" after a few days of therapy had an electrolyte loss pattern similar to those with hypertension. They decreased their urinary electrolyte loss while they were edema-free and on the low-salt diet. The diuresis of electrolytes returned in all during the Out-Patient Department follow-up period and greater losses were evident than during their baseline observation period.

Several patients were studied who had edema refractory to ordinary methods of treatment. When hydrochlorothiazide was given alone, a slight diuresis was achieved. When the drug was given along with a mercurial diuretic, a further, much larger diuresis was produced. In one patient, hydrochlorothiazide was given three times a week and was followed by meralluride, cc. intramuscularly in order to

produce a maximum diuresis. In another patient with refractory edema, hydrochlorothiazide was given daily and meralluride was required about every seven to ten days.

Side Effects

None of the patients in the study developed toxic reactions to the drug. No skin reactions, gastro-intestinal disturbances, or changes in the white blood count or differential leucocyte count were noted.

Two significant side effects were observed during the study. Although the K diuresis with this drug is only slight—10-20 mEq. per day—it is a continual and persistent occurrence. Several of the patients described weakness and easy fatigability after several weeks on the drug. Although serum K levels were normal in these patients, their symptoms disappeared when K supplements were given. It is therefore advisable to recommend an increased K intake in the form of food, i.e., orange juice, at the onset of drug therapy, rather than to wait until symptoms appear and then give medications. The depletion of K is probably a gradual cumulative effect of the slight increased daily K loss.

All patients given hydrochlorothiazide are put in a relative low-salt state. Those patients who are given the drug and who are free of edema may develop some degree of dehydration. This is evident by a rise in both the hematocrit and NPN. Patients with normal kidney function will rapidly compensate and no complications will develop. On the other hand, those patients with renal disease may be thrown into frank uremia if the drug is continued. For this reason, patients who have azotemia, or other evidence of renal disease, should be given the drug only with extreme care. A steady and progressive rise in the NPN calls for discontinuation of therapy.

An Approach to Treatment of Essential Hypertension

Most of the many methods available for lowering the blood pressure in patients with essential hyptertension are cumbersome, require combinations of drug therapy, and it takes months to achieve maximum control. We have found the following method to be useful in many such cases in simply and rapidly controlling the blood pressure. The patients are placed on a low-salt diet or a no-salt liquid formula diet such as Controlyte.* Along with this, or after a few days on the special diet, one of the chlorothiazide group of drugs is administered. If the

*The Dietene Company, Minneapolis.

method is effective, significant lowering of the blood pressure should occur within one week. When reduction of the blood pressure is maximal, the patient should be returned to an unrestricted diet and the chlorothiazide drug should be continued. This will produce an "exogenous low-salt diet" and will allow the patient to be in a relatively low-salt state despite general food intake. Any subsequent rise in pressure may then be treated by a temporary return to either the low-salt diet or the liquid formula, until the pressure is again controlled. The majority of cases which we have treated in this fashion have had a smooth and rapid reduction in their pressure and have maintained this with a minimum of medication and inconvenience.

Use in Edema States

There is no question that drugs of the chlorothiazide group are very valuable agents in the treatment of edema states due to sodium retention. The edematous patient responds to chlorothiazide, not only by an increase in total volume of urine with a subsequent increase in total urinary sodium, but also by an increased concentration of Na in this increased volume. We have noted 24-hour urinary Na levels as high as 600 mEq in edematous patients treated with the drug. Again this diuresis of Na and H_2O can be aided by a low- or no-salt diet and again, once dry weight is achieved, the "exogenous low salt diet" described previously can be used to control milder cases. This permits the patient to eat a palatable diet and yet be in a low-salt state. Many patients who previously required mercurial injections weekly, can now be maintained on oral hydrochlorothiazide without a need for injections and, finally, those patients with refractory edema may develop a diuresis when hydrochlorothiazide is used along with some other diuretic agent.

Conclusions

The drugs of the chlorothiazide group are effective agents in the treatment of edema states due to Na retention and in many patients with essential hypertension. Hydrochlorothiazide is a derivative of chlorothiazide which is effective in doses one-tenth that of chlorothiazide. Although no toxic effects are noted with the drug, care should be taken in giving it to patients with renal disease, and K supplements should be administered with the drug to prevent K depletion.◀

original article

Evaluation of Combined Prednisone-Phenylbutazone Therapy in Arthritic Disorders

EDWARD SETTEL, M.D.,* *Forest Hills, New York*

►*Since cortisone was first used as an agent in the treatment of arthritis, several derivatives have been developed and introduced to improve its characteristics while diminishing the side effects. This combination brought complete relief in 58 per cent of the patients tested and marked relief in an additional 32 per cent.*◄

It is now almost a decade since the first reports of the value of cortisone in rheumatoid arthritis made their appearance. For a brief period, hope was high that at last a therapy had been found which would permanently halt the progress of the disease and in a great measure restore the patient's former functional capacity. Unfortunately, as experience was acquired, evidence has accumulated that the benefits to be derived from long-term steroid therapy are gained only at measurable risk.

Over the years intervening since the synthesis of cortisone, intensive research has led to the development of several derivatives which have been considered of sufficient merit to introduce into practice: hydrocortisone, prednisone, prednisolone, triamcinolone, methylprednisolone and, most recently, dexamethasone. The synthesis of these compounds must be considered highly successful in the sense that vast increase in potency has been achieved. However, in none of them has therapeutic benefit been divorced completely from risk of hypercortisonism, and long-term steroid treatment must still be regarded as fraught with serious hazards.

The gravity of this problem is reflected in the high incidence of side reactions. Forty-one different untoward effects in 68 patients observed over 5 years have been reported. The total number of undesirable incidents in this

*Forest Hills Nursing Home, Forest Hills, New York.

group was 404.[1] Other workers[2] have suggested that 66 to 75 per cent of patients on long-term adrenal steroid therapy develop symptoms of hypercortisonism.

General experience, it is believed, would confirm the observation that the risk of deleterious side effects increases with the size of dose prescribed. In this view a daily maintenance dosage of prednisone exceeding 15 mg. (and presumably the therapeutically equivalent dose of any congener) holds great risk of producing major undesirable side effects.[3]

Any measure, therefore, which tends to reduce the patient's steroid requirements without significantly detracting from the therapeutic effect is most desirable. In this connection, a number of investigators[4-7] have reported that supplementation of hormonal therapy with phenylbutazone allows a reduction in hormone dosage without detriment to the therapeutic result. Two investigators[7] found that they could add to the patient's comfort "more smoothly" with the combined medication than with the hormone alone.

1. Howell, D. S., & Ragan, C., *Medicine*, 35: 83, 1956.
2. Rotstein, J., & Good, R. A., *A.M.A. Arch. Int. Med.*, 99:545,1957.
3. Bunim, J. J., *Bull. N.Y. Acad. Med.*, 33: 461,1957.
4. Kuzell, W. C., et al., *Arch. Int. Med.*, 92: 646,1953.
5. Nelson, S., *Bull. Post-Grad. Comm. Med., Univ. Sydney*, 10:80,1954.
6. Strandberg, B., *Brit. J. Phys. Med.*, 19:9, 1956.
7. Platt, W. D., Jr., & Steinberg, I. H., *New England J. Med.*, 256:823,1957.

A number of their patients who had been taking an excessive maintenance dose of prednisone were switched to the combination without disturbance. Only during major exacerbations was it necessary to temporarily increase its hormone dosage.

Material and Method of Study

A total of 34 patients was selected for treatment with the new drug combination.* Twelve were permanent inmates of a well-equipped nursing home with excellent facilities for constant observation and control. The remainder were drawn from private practice. There were 15 men and 19 women, age ranging from 32 to 89 years. All were subjected to complete physical examination at the beginning and end of treatment and attended for check-up at frequent intervals during therapy. Since, in our opinion, the combined therapy was of potential value in both acute and chronic conditions, cases were selected to provide a cross-section of the arthritic disorders most commonly encountered in practice. (Table 1).

In acute disorders 2 capsules q.i.d. were administered for two days and half this dosage for the next two days. Thereafter on

*Sterazolidin®, each capsule contains prednisone 1.25 mg., phenylbutazone 50 mg., aluminum hydroxide 100 mg., magnesium trisilicate 150 mg., and homatropine methylbromide 1.25 mg. Geigy Pharmaceuticals, Ardsley, N. Y.

RESPONSE OF VARIOUS ARTHRITIC DISORDERS TO *STERAZOLIDIN* THERAPY

Disease	Number of Patients	Response		
		Excellent	Good	Poor
Acute Disorders:				
Acute traumatic or idiopathic low back pain	5	3	2	—
Acute traumatic muscular or ligamentous injury	2	2	—	—
Acute subdeltoid bursitis	3	2	1	—
Chronic Disorders:				
Lumbo-sacral osteoarthritis	3	1	1	1
Sacro-iliac osteoarthritis	3	2	1	—
Cervical osteoarthritis	2	1	1	—
Osteoarthritis of the knees or hips	4	1	2	1
Rheumatoid arthritis	9	6	2	1
Totals	31	18	10	3

capsule t.i.d. or b.i.d. was given until symptoms were completely controlled for a period of at least three consecutive days. In chronic disorders 2 capsules were administered q.i.d. for a week. During the succeeding two weeks half this dosage was administered whenever necessary; thereafter one capsule t.i.d. until complete relief was obtained for at least one week. Subsequent maintenance dosage for continued control was stabilized at one capsule b.i.d. Thus maximum daily dosage of prednisone, even for the briefest period, never exceeded 10 mg.

The response was graded as "excellent" when complete relief was achieved; as "good" when relief was marked, but not complete; as "poor" when there was little or no relief of symptoms.

Complete relief of symptoms was obtained in 58 per cent of patients, marked relief in an additional 32 per cent. Thus 90 per cent in all gained worthwhile improvement, and only 10 per cent failed to show response. Generally, pain was the first symptom to be relieved. Often within 2 to 3 days the patient expressed complete freedom from discomfort. Within a brief period thereafter the range of joint motion was increased and swelling, edema and effusion gradually subsided. Two patients who failed to continue therapy complained of return of symptoms within five days and presented themselves for resump-

she calls it "nervous indigestion"

diagnosis: a wrought-up patient with a functional gastrointestinal disorder compounded by inadequate digestion. **treatment:** reassurance first, then medication to relieve the gastric symptoms, calm the emotions, and enhance the digestive process. **prescription:** new Donnazyme—providing the multiple actions of widely accepted Donnatal® and Entozyme®—two tablets t.i.d., or as necessary.

Each Donnazyme tablet contains

—In the gastric-soluble outer layer: Hyoscyamine sulfate, 0.0518 mg.; Atropine sulfate, 0.0097 mg.; Hyoscine hydrobromide, 0.0033 mg.; Phenobarbital (1/8 gr.), 8.1 mg.; and Pepsin, N. F., 150 mg. **In the enteric-coated core:** Pancreatin, N. F., 300 mg., and Bile salts, 150 mg.

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tion of therapy.

A control study was conducted on 10 patients using prednisone alone as the only oral therapy. Five patients with acute low-back syndrome and five suffering a recurrence of osteoarthritis were designated for this phase of observation, and the dosage of the corticosteroid was doubled over that used, i.e., 2.5 mg. in each tablet. For the first four or five days of treatment, two such tablets (a total of 5 mg.) was administered in each dose. Then the dosage was cut in half for a similar period, and finally reduced gradually until full withdrawal.

In this control series, it took 4 to 5 days of therapy initially with prednisone alone to achieve the same level of relief provided by this combination in 2 to 3 days.

Twelve patients who were maintained on therapy for 8 to 14 weeks continuously were subjected to hemograms and renal and hepatic profiles at the onset and conclusion of therapy. No changes significant of toxicity were noted. One patient on long-term therapy complained of mild gastric discomfort during the fifth week, but, because of the excellent relief afforded, refused to discontinue medication. The annoying symptoms subsequently subsided spontaneously.

Case Reports

Case 1

A woman of 77, suffered from recurrent bouts of osteoarthritis of the knees and lumbar spine for 12 years, each attack lasting from five to 10 weeks, and causing pain and disability. Between attacks there remained stiffness of the knees, enlargement of the joint, and marked restriction of all motion in the lumbar spine. In addition, she exhibited evidence of arteriosclerosis and moderately advanced cardiovascular disease well-controlled with digitalis and occasional mercurial diuretics.

The present episode was another bout of severe pain, swelling and restriction of flexion and extension in both knees and lumbar spine. The patient had great difficulty in walking, but no fever.

She was started on two capsules of the prednisone-phenylbutazone combination q.i.d. for the first week one capsule q.i.d. the next two weeks. Following this the dosage was gradually tapered off so that by the fourth week she was able to discontinue medication.

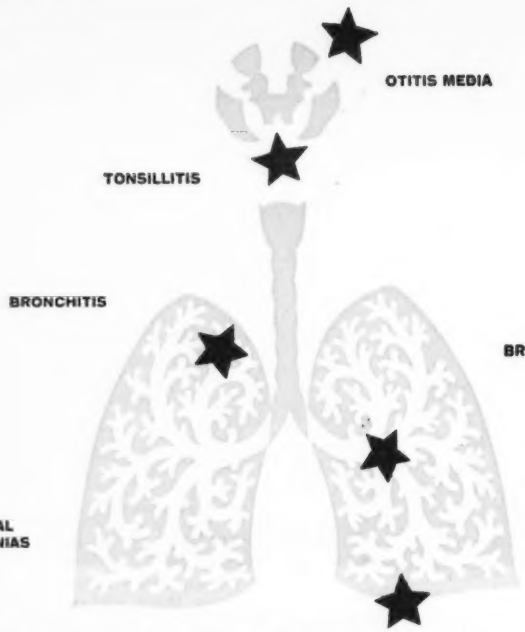
Within three days of the onset of therapy there was a rather dramatic subsidence of pain, swelling and discomfort. She was able to walk with ease and felt that this was the most rapid relief she had ever had from any medication. By the sixth day the symptoms had completely abated, but the medication was continued on a gradually decreasing dosage for several weeks thereafter.

There were no side effects of any type, nor any alteration in the hemogram, or renal or hepatic profile.

Case 2

A man of 37, was seen the day after the acute onset of agonizing pain in the sacro-iliac area, when he attempted to lift a heavy piece of furniture. He walked with his body bent laterally in a rigid position and winced with each step. Examination revealed acute spasm of the lower lumbar muscles and complete inability to flex, extend or rotate the spine.

This patient was put on two capsules of the prednisone-phenylbutazone combination q. 4 h. for two days,



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1. Lysaught, J. N., and Cleaver, W.: Proceedings of the Detroit Symposium on Antibacterial Therapy (Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959).

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then one capsule q. 4 h. for two days, and the dosage gradually tapered off over the next week.

After 36 hours of therapy relief of spasm was better than 60 per cent, and walking was far less painful and difficult. At the end of the second day he felt 90 per cent better and returned to work. All symptoms and signs of spasm of the musculature of the low back disappeared. By the fourth day he was completely asymptomatic.

CASE 3

A man of 53 had a 6-year history of recurrent bouts of rheumatoid arthritis. The present attack involved the right wrist and left shoulder—redness and swelling of both joints, temperature 101°, S.R. 43 mm. per hour, white count 20,500, with a slight shift to the left.

The patient was put on two capsules of prednisone-phenylbutazone combination q. 4 h., for five days, the dosage then gradually reduced over a period of two weeks. After three days of therapy the redness and swelling of the two joints had diminished markedly and the patient was able to move the involved wrist and arm with a minimum of pain. The temperature subsided by the fourth day, and appetite returned.

Within a week of the onset of therapy the symptomless patient was able to leave his house. He returned to work the next week and continued the low dosage for a period of two weeks. There were no signs of toxicity, no side effects.

Summary and Conclusions

1. Combined medication with prednisone and phenylbutazone has been evaluated in treating 31 patients manifesting a variety of acute and chronic arthritic disorders.

2. Complete relief of symptoms was obtained in 58 per cent and marked relief in an additional 32 per cent. No side effects of any significance were noted and no objective evidence of toxicity detected.

3. Prednisone and phenylbutazone in combination appear to offer definite therapeutic advantages. It is my impression that the response in acute conditions is more rapid than that seen with either agent used alone. In chronic disorders the phenylbutazone component sharply reduces hormone requirement so that adequate control can be maintained with little or no danger of the induction of hypercortisonism.◀

Celiac Disease: Faulty Metabolism of Gluten

Treatment of celiac disease has been simplified and prognosis improved by the discovery that wheat and other grains are the noxious agents. Studies indicate that the harmful component is the gliadin fraction of gluten. The action of gliadin may be related to glutamine-containing peptides not split into amino acids, these having an abnormal effect on metabolism.

Weijers, H. A., & van de Kamer, J. H., *Pediatrics*, 25:127-134,1960.

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Indications for Surgery in Arterial Disease

W. STERLING EDWARDS, M.D.,* *Birmingham, Alabama*

Recent advances in surgical techniques have made it possible to rehabilitate and prolong the lives of many patients with arterial damage. Once the nature of the aneurysm or the obstruction has been determined and the limitations of the procedure realized, the physician may proceed with surgery.

With the development in the past decade of techniques for replacement of damaged or diseased arteries, first with homografts and more recently and more satisfactorily with synthetic tubes, many patients with arterial disease can now be helped. Crippled persons can be restored to an active life, and death from ruptured aneurysms can be prevented by removing dilated segments of diseased arteries. It is important for all physicians, therefore, to be aware of the indications, contraindications, and limitations of arterial surgery at the present time.

Aneurysms

Thoracic aneurysms due to syphilis have markedly decreased in frequency in the past few years since penicillin has almost wiped out this disease. Today many more thoracic aneurysms are fusiform and result from degenerative changes of arteriosclerosis. These may cause symptoms by pressure on the bony thoracic cage, the trachea or esophagus, and may paralyze the left recurrent laryngeal nerve by expansile pressure. If the thoracic aneurysm is limited to the descending aorta distal to the left subclavian artery, it can be removed and replaced with a graft with relative safety. If the aneurysm is proximal to the left subclavian artery and involves the ascending or transverse aortic arch, the operation is a much more formidable procedure with a very high mortality, even in the most experienced hands. In the ascending and transverse arch, only progressive or severe symptoms warrant the very hazardous surgery necessary. On the other hand, relatively small aneurysms

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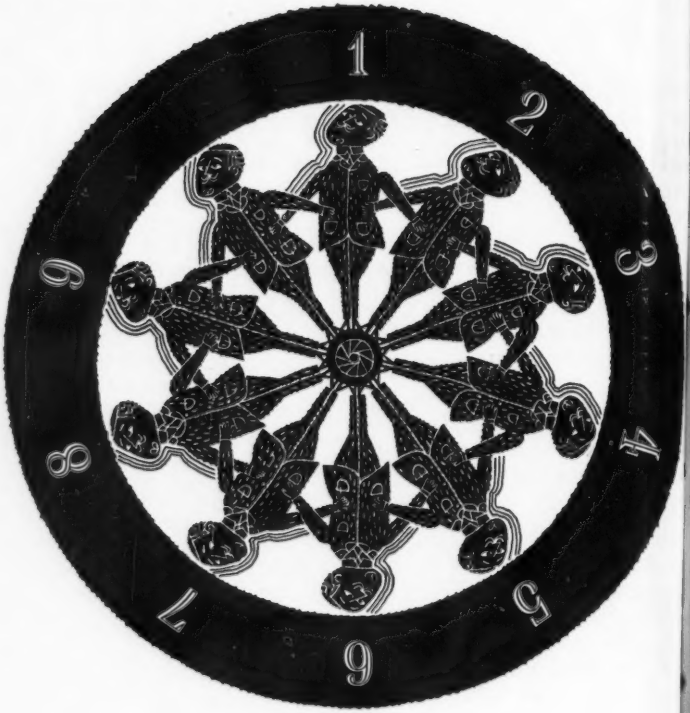

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References: 1. Menger, H. C.: Clin. Med. 4:313 (Mar.) 19[illegible] 2. Seal, J. C.: Eye Ear Nose & Throat Month. 38:715 (Sept.) 1959.

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of the descending aorta, should be resected and replaced in patients with an otherwise good prognosis. The previous complications from clamping the aorta in this area, chiefly spinal cord damage and renal injury from temporary ischemia, have been overcome by the use of a pump which removes blood from the left auricle through plastic tubing and supplies this blood under arterial pressure to the femoral artery. Thus, while the aorta is cross-clamped the spinal cord and the intra-abdominal organs are receiving a sufficient quantity of oxygenated blood.

Diagnosis

Abdominal aortic aneurysms are easily diagnosed by palpation of an expansile mass or by observing a circular calcific shadow on the abdominal x-ray film. If this aneurysm is not causing symptoms it is still dangerous: 85 per cent of these individuals will be dead from rupture within three years. For this reason all patients with a definite diagnosis of abdominal aortic aneurysm should be operated on, provided they do not have severe heart disease or severe renal disease. If the patient's life expectancy is three to five years aside from the aneurysm, then surgery should be advised. Mortality from operation is now at a quite acceptably low rate of 5 to 10 per cent in most clinics.

Symptoms of back pain or abdominal pain already manifested is an ominous warning, indicating dissection occurring within the aortic wall and danger of impending rupture. The mortality within six months if nothing is done is close to 100 per cent. Even after the aneurysm leaks, an occasional patient can be saved, especially if the leak is posterior into the closed retroperitoneal space. Here pressure builds up and temporarily stops bleeding. The patient will suffer severe back pain but will not die from shock for a few hours or days. Emergency surgery is indicated and some 30 per cent of patients can be saved.

Popliteal artery aneurysms have a more favorable prognosis, since rupture in this location seldom leads to fatal hemorrhage. The chief danger is thrombosis with irreversible ischemia of the foot, requiring amputation. Even asymptomatic aneurysms in the popliteal area should be excised, because experience has demonstrated that within two or three years a great majority will become complicated by thrombosis or rupture. Here again the removal of the aneurysm with replacement by a synthetic graft is a very satisfactory procedure with a low morbidity and mortality.

Arterial Obstruction

Although it is well known that arteriosclerosis is a generalized disease, it has recently been realized that the symptoms may be due to segmental involvement of arteries in quite localized areas. This is particularly true of involvement of the arteries to the legs. The abdominal aorta just proximal to the bifurcation, the common iliac, the superficial femoral, and the popliteal arteries are those, segmental involvement and occlusion or stenosis of which may cause symptoms of ischemia. As a segmental area to the legs becomes occluded the patient first notices claudication or pain in a muscle group below the block produced by walking one-half to several blocks. The pain is relieved in minutes after stopping walking even though the patient remains standing. At first there are no trophic changes of the feet—no rubor on dependency, no loss of hair or hypertrophy of the nails. These symptoms occur only if the lesion progresses and more and more of the collaterals around the block become occluded by atheromatous material. Therefore, the best candidates for surgery are those with claudication and no evidence of trophic changes. Very mild claudication brought on only by walking four or five blocks in a patient who does not need to walk this distance for making a living is not an indication for surgery. More severe claudication, e.g., at one-half to one block, or pain severe enough to interfere with a patient's work indicates operation. Another indication is progression of symptoms. A patient with mild claudication may notice that his walking tolerance is rapidly decreasing, in which case surgery should be immediately advised. Many patients with impending, or actual onset of, gangrene can have a leg salvaged by an arterial graft. Grafts can bridge gaps as long as 20 inches from the abdominal aorta to the popliteal artery below the knee. The main requirement for a successful operation is that there be an open artery of adequate size below the block. Below the knee and beyond the popliteal bifurcation, vessels become too small for suturing grafts and, therefore, this at the present time is a lower limit. It appears that any patient with severe claudication, progressive claudication, or impending or early gangrene should have a lumbar aortogram or a femoral arteriogram to see if a segmental occlusion exists which can be bypassed with a graft. No leg should be amputated without first making sure that a successful grafting is impossible.

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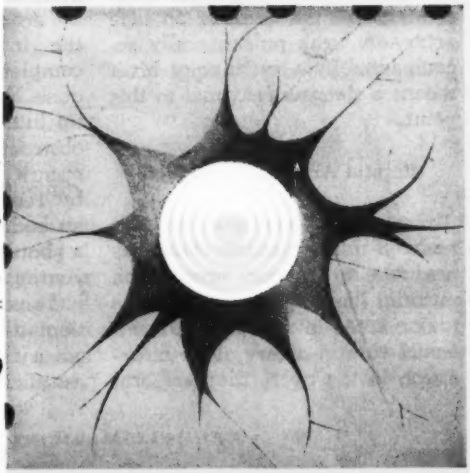

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familiar calf fatigue on walking produced by femoral obstruction. Obstruction of the abdominal vessels causes pain in one or both gluteal muscle groups in the lower back, posterior thigh and calf muscles. Diminished blood flow to the genitalia in males prevents maintenance of erection and so interferes with sexual indulgence. Frequently the pain of back, hip and thigh claudication is mistaken for sciatic compression by a ruptured lumbar disc. The distribution of pain is the same in the two conditions, but the pain of the lumbar disc is aggravated by shifting position or straight-leg raising, whereas, only walking will produce the pain of arterial insufficiency. The examination of the femoral, pedal and popliteal pulses is extremely important in cases of this type. A complete obliteration of the femoral pulses means a complete obstruction of the aorta or an iliac artery. A weak pulse usually accompanied by a murmur or bruit means a stenosis proximal to this point.

Carotid Artery Obstruction

Even more recently it has been realized that a number of strokes are due to arterial obstruction outside the cranial cavity. The major areas involved are the internal carotid artery at its bifurcation in the neck, the vertebral artery where it arises from the subclavian artery in the thorax and the origin of the common carotid artery from the aortic arch or innominate artery inside the chest. Many patients with extracranial arterial obstruction or stenosis will present with transient episodes of arm and leg weakness on the side opposite the stenosis, blurring of vision, or vague visual disturbances on the same side as the obstruction. Transient dizzy spells due to basilar artery insufficiency may mean that the vertebral artery is practically occluded. A different blood pressure reading in the two arms and unequal strength of the carotid pulses may indicate obstruction of the innominate and the common carotid arteries. Any patient with transient episodes of hemiparesis should be advised to have early study of the arterial circulation to his brain by arteriography. If the block of the internal carotid artery is complete, often nothing can be done because the block extends up into the cranium. If a partial obstruction of the internal carotid occurs, a great deal can be done by removing the obstruction by an endarterectomy or graft with a simple operation, thereby preventing the occurrence of complete paralysis. A number of patients have made dramatic recovery from symptoms of arterial insufficiency, but after a con-

plete stroke the brain damage may be irreversible in a few hours. Therefore, once a patient has complete paralysis, emergency surgery may be indicated, but only an occasional patient will be improved.

Renal Artery Obstruction

Any individual under 20 with hypertension and anyone over 50 with sudden onset of hypertension should be studied for unilateral renal artery stenosis. The Goldblatt phenomenon may be produced by congenital stricture of the renal artery or by the development of an arteriosclerotic plaque at the branching of the artery from the aorta. Poor or delayed diodrast excretion on one side during intravenous pyelography suggests this lesion. Further studies to confirm unilateral renal artery stenosis are:

1. Decreased minute volume flow and sodium excretion on one side as determined by retrograde ureteral catheterization.

2. A difference in radioactive diodrast uptake of the two kidneys, using a separate scintillation counter over each kidney.

If all these tests definitely suggest a difference in renal blood flow on the two sides, lumbar aortography should be done to visualize the renal arteries. In many cases the lumen of the renal artery can be reconstructed by endarterectomy or graft, if not, and the opposite kidney has normal function, a nephrectomy will reduce pressure to normal.

Summary

A rapidly increasing number of organs or limbs of the body have been found to be susceptible of restoration to full function if the arterial blood supply can be reconstructed. Arteriosclerosis is the chief cause of arterial obstruction and until such time as prophylactic or curative medical treatment becomes available, arterial surgery offers the only hope of rehabilitation.◀

Kanamycin Sulfate: Ototoxicity in the Presence of Compromised Renal Function

Of 2 men aged 40 and 48 whose hearing was severely damaged after small doses of kanamycin sulfate (Kantrex), each had had a nephrectomy placing them in a stage of compromised renal function even though urinary output was adequate. Potentially ototoxic drugs should be used with great caution, particularly in patients whose renal function may be vulnerable.

Naunton, R. F., & Ward, P. H., *A.M.A. Arch. Otolaryng.*, 69:398-399,1959.

Orally Administered Trypsin: A New Concept in Enzyme Therapy

ROBERT H. G. MONNINGER, M.D.,* *Lake Forest, Illinois*

►*Evaluation of orally administered trypsin in 72 cases of various ocular disorders indicates that this agent has effective anti-inflammatory activity and a wide margin of safety. It has been shown to be of value in combating edema and attendant inflammation resulting from traumatic injury and/or surgery to the eye.*◄

Trypsin is a hydrolytic, proteolytic enzyme. Schepowalnikow was the first to show that this proteinase was activated from its precursor trypsinogen by enterokinase in the small intestine. Its optimum pH is 8. Trypsin breaks proteose and peptone fragments of protein molecules into smaller amino acid groups or peptids. It acts on peptide linkages containing the carboxyl group of lysine or arginine, and its hydrolytic action on synthetic substrates requires the presence of such residues. This enzyme has fibrinolytic and mucolytic properties. The antiphlogistic propensity of trypsin could be due to fibrinolysin activation, depolymerization and reversal of the fibrinogen-fibrin reaction, or inhibition of polypeptide formation. A combination of these mechanisms acting simultaneously is also possible.

The ability of trypsin to affect permeability was demonstrated in laboratory animal intracutaneous dye-spreading tests. This is likely facilitated through enzymatic depolymerization of macro-molecular protein moieties, and subsequent removal of denatured materials. Such a process of decongestion of the lymphatic and capillary pores would reduce the viscosity of edema fluid and increase focal drainage. It is also regarded to act as an esterase, polymerase, and transaminase, and it decreases the hypersensitivity reaction. In the egg-white edema reaction of Selye, trypsin was found to be more effective than cortisone in reducing edema both in regard to pre-treatment and protection.

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It is effective in varying degrees in combating inflammation and edema due to allergic, bacterial, chemical and viral agents. (Of itself, however, it has no antibacterial property). It does not act by fever induction, and the concept of thrombolysis has been refuted.

There is a growing list of published clinical experiences on the use of trypsin therapy. One review discusses the value of this modality to reduce edema and inflammation attendant with various clinical entities.[1] Controlled studies have established the use of trypsin therapy in thrombophlebitis.[2-4] Experiences with intramuscular trypsin in the management of several ocular disorders have been reported.[5-7] Its value in treating traumatic and infective inflammation and edema of the head and neck has been observed.[8]

It has been shown that the enzyme could be absorbed through the buccal pouch.[9-11] Its use topically in unguentine form to treat ocular conditions has been reported.[12]

The feasibility of obtaining intestinal absorption of trypsin was demonstrated when radioactive tagged trypsin, placed into an isolated section of the gut of animals, was absorbed through the intestinal mucosa and appeared in the blood stream.[13,14] This was accomplished by attaching I^{131} to trypsin and then testing circulating blood for radioactivity. There was no concentration at the thyroid gland which indicated that the iodine remained attached after absorption and that the entire molecule or at least a part of it, transferred across the mucosa. As a follow-up, tablets were made available for clinical trial which contained trypsin 20 mg.* and which were coated to prevent dissolution in the acid region of the gut.

The enteric tablet is easy to take, and eliminates such reported side reactions as pain and induration at the injection site or mucosal irritation using intramuscular or buccal enzyme. The drug is used with similar effect as the latter two forms in traumatic injuries, surgical pro-

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*Orenzyme® (Enteric Coated) 20 mg. tablets. The National Drug Co., Philadelphia.

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cedures, and various inflammatory conditions. It is not known how much of the enzyme absorbed is active. It is suspected that it is of a fragmentary magnitude and this underlines the importance of using large dosages.

Methods and Tolerance

This study consists of 72 patients who were placed on tablets containing 20 mg. trypsin each. The average dosage was two tablets initially and one tablet every four hours thereafter. Of the 72 cases, 47 were traumatic in nature due either to injury or surgical procedure; 5 were protracted cases of uveitis; 12 were inflammatory and edematous conditions of the external eye and adnexa; and 8 were retinopathies.

Ages of the patients treated varied from 4 to 81 years. Duration of therapy usually was a matter of days to a week as indicated, but several of the subjects were on the medication for months. In no instance was there untoward side reaction to the drug, nor did it have to be discontinued because of incompatibility with other drugs. Its effect was evaluated by comparing the course of a disease with and without use of the enzyme.

Review of Cases

Six of the patients had enucleations. In surgical cases, trypsin was given one day before surgery and for as long as indicated postoperatively. The clinical recovery time, based on reduction of edema and discoloration, was decreased in each instance of enucleation. This allowed for an earlier prosthesis application. Growths, including cysts, papillomas and malignancies, were excised in 16 cases. Some of the procedures involved rather extensive plastic repair. Use of the enzyme in these cases reduced attendant postoperative edema and induration.

Injuries to the eyes of 10 patients were due to forcible contact with blunt objects. The usual attributes of pain, swelling and discoloration were noted to subside rather rapidly. One case was a commotio retinae (concussion edema) involving mostly areas of the macula and optic disc. Edematous rucks were present. Good central vision returned in this patient within 10 days. No permanent changes about the macula were noted. Another patient, incurring a thermal injury, showed early debridement and sloughing of the burned areas. There was also early exposure of healthy tissue and lack of severe scarification or secondary infection.

Five cases of dacryocystitis were treated with the enteric-coated enzyme and antibiotics.

One of the cases was acute, the others were chronic. Two of these patients were young children. The resolution time in this cases was impressively enhanced, and discoloration and edema, so often present after probing, did not occur.

Dacryocystorhinostomy was performed on one patient subsequently and the postoperative course was mild and without sequelae. A stab incision was required in one case in which the recovery was rapid and orderly.

Ten intracapsular lens extractions were observed using trypsin in conjunction with the usual ancillary medications. Postoperative iritis was not as severe, nor did it persist as long, as in some cases wherin the enzyme was not employed.

The oral enzyme was given to 5 patients with a history of chronic uveitis. All of these patients had been given fever and/or cortisone treatment at one time in the past along with topical antibiotics, cortisones and mydriatics. No dramatic changes resulted in the cases treated with the enzyme. It was felt that trypsin would be a safe form of medication as an adjuvant in long-term therapy, especially in diabetics where cortisone is likely to worsen the diabetic state; in debilitated persons who could not tolerate fever therapy; and in TBC and viral disease. One of the patients was on the drug for 16 months.

The 12 patients with inflammation and edema of the adnexa and globe surface presented an interesting group. In two instances a secondary infection was present and an antibiotic ointment was also used. Antihistamines, trypsin and cold compresses were administered to 10 subjects. In 24 to 48 hours the edema and pain were gone. Two of the group had herpetic keratitis—one H. zoster ophthalmicus, the other H. simplex. Scleritis attended these cases. The patient with the H. simplex was placed on mydriatics, trypsin and antibiotic drops. Clinical recovery and return of normal visual acuity occurred in ten days. The H. zoster ophthalmicus case was placed on a regimen of enzymes, combined with biotic and cortisone drops, and mydriatics. A slight impairment of visual acuity existed after recovery.

Retinopathies in the group of 8 patients included disciform degeneration of the macula (Junius-Kuhnt) in 2, diabetic retinal changes in 2, occlusion of a central retinal artery in 1, arteriosclerotic changes in 1, Eale's disease in 1, and traumatic vitreous hemorrhage in 1. One case of Junius-Kuhnt disease was treated by another physician who placed the patient on the oral enzyme

and reported progress regarding diminution of the exudate and hemorrhage, but little recovery of vision. One of the two diabetic patients had grade IV changes of long standing, secondary glaucoma, lens opacification, and equivocal light perception. No changes of consequence were noted on a short course of therapy, and it was discontinued by mutual consent. The patient with retinal artery occlusion was treated with paracentesis, vasodilators, and trypsin. Edema and fundal detail were improved, and recovery of vision amounted to some recognition of distant objects and forms. One case with long standing retinal arteriosclerotic changes failed to show conspicuous improvement. One patient with Eale's disease and another with traumatic vitreous hemorrhage were characterized by early reabsorption of the vitreous blood. Since this might be the case in untreated eyes, the effect of the drug was viewed with reservation.

Illustrative Cases

Case 1

A woman of 56 is an arrested tubercular, an arthritic, and an established diabetic with retinal changes of 5 years' duration, including recurrent vitreous hemorrhages. She had been under the care and observation of three ophthalmologists and an internist before the author saw her in consultation one year ago. Treatment in the past included diet control, insulin standardization, vitamins K and C, and testosterone and various forms of medication for the arthritis. A hypophysectomy had been recommended by another physician. Examination revealed numerous exudates, punctate and paracentral hemorrhages, neovascularization, mesoblastic fibrous proliferation into the vitreous originating from the area of the disc, vasculitis and scleroses in O.U. Her corrected vision was: R.E., 20/50-, L.E., 20/400. Visualization was not good in either eye. Except for some cortical lens changes, the remainder of the examination was non-contributory. Medication for the year following examination, regulated and administered by her physician, was as follows: a combination containing per tablet ergotamine tartrate 0.3 mg., total levorotary alkaloids of belladonna 0.1 mg., and phenobarbital 20 mg. 1 tablet q.i.d., meprobamate 400 mg. 1 tablet q.i.d., chlorothiazide 0.50 mg./day, KCl 1 gm./day, ethinyl estradiol 0.05 mg./day, insulin 30 US NPH plus 5 US PZI, a combination containing per capsule hesperidin complex 100 mg. and vitamin C 100 mg. 3 capsules q.i.d., atheromatosis product 2 capsules q.i.d., Orenzyme 2 tablets q.i.d., vitamin K 5 mg./day, and therapeutic dosages of vitamin B_{12} I.M. daily. On two occasions in the past, steroid therapy had been tried and discontinued because her diabetic status worsened and there was increased water retention.

Eleven months later the patient was again seen in consultation. The condition of the fundi was vastly improved and the retinitis was in a stage of remission. Her vision was correctible to: R.E., 20/20-, L.E., 20/15-. A staff ophthalmologist had seen her shortly before my examination and had noted that her retinopathy was adequately controlled.

Case 2

A physician of 42 presented himself for examination and treatment. Some ten days previously he had an attack of herpes labialis which appeared to

One of the cases was acute, the others were chronic. Two of these patients were young children. The resolution time in this cases was impressively enhanced, and discoloration and edema, so often present after probing, did not occur.

Dacryocystorhinostomy was performed on one patient subsequently and the postoperative course was mild and without sequelae. A stab incision was required in one case in which the recovery was rapid and orderly.

Ten intracapsular lens extractions were observed using trypsin in conjunction with the usual ancillary medications. Postoperative iritis was not as severe, nor did it persist as long, as in some cases wherin the enzyme was not employed.

The oral enzyme was given to 5 patients with a history of chronic uveitis. All of these patients had been given fever and/or cortisone treatment at one time in the past along with topical antibiotics, cortisones and mydriatics. No dramatic changes resulted in the cases treated with the enzyme. It was felt that trypsin would be a safe form of medication as an adjuvant in long-term therapy, especially in diabetics where cortisone is likely to worsen the diabetic state; in debilitated persons who could not tolerate fever therapy; and in TBC and viral disease. One of the patients was on the drug for 16 months.

The 12 patients with inflammation and edema of the adnexa and globe surface presented an interesting group. In two instances a secondary infection was present and an antibiotic ointment was also used. Antihistamines, trypsin and cold compresses were administered to 10 subjects. In 24 to 48 hours the edema and pain were gone. Two of the group had herpetic keratitis—one H. zoster ophthalmicus, the other H. simplex. Scleritis attended these cases. The patient with the H. simplex was placed on mydriatics, trypsin and antibiotic drops. Clinical recovery and return of normal visual acuity occurred in ten days. The H. zoster ophthalmicus case was placed on a regimen of enzymes, combined antibiotic and cortisone drops, and mydriatics. A slight impairment of visual acuity existed after recovery.

Retinopathies in the group of 8 patients included disciform degeneration of the macula (Junius-Kuhnt) in 2, diabetic retinal changes in 2, occlusion of a central retinal artery in 1, arteriosclerotic changes in 1, Eale's disease in 1, and traumatic vitreous hemorrhage in 1. One case of Junius-Kuhnt disease was treated by another physician who placed the patient on the oral enzyme

and reported progress regarding diminution of the exudate and hemorrhage, but little recovery of vision. One of the two diabetic patients had grade IV changes of long standing, secondary glaucoma, lens opacification, and equivocal light perception. No changes of consequence were noted on a short course of therapy, and it was discontinued by mutual consent. The patient with retinal artery occlusion was treated with paracentesis, vasodilators, and trypsin. Edema and fundal detail were improved, and recovery of vision amounted to some recognition of distant objects and forms. One case with long standing retinal arteriosclerotic changes failed to show conspicuous improvement. One patient with Eale's disease and another with traumatic vitreous hemorrhage were characterized by early reabsorption of the vitreous blood. Since this might be the case in untreated eyes, the effect of the drug was viewed with reservation.

Illustrative Cases

Case 1

A woman of 56 is an arrested tubercular, an arthritic, and an established diabetic with retinal changes of 5 years' duration, including recurrent vitreous hemorrhages. She had been under the care and observation of three ophthalmologists and an internist before the author saw her in consultation one year ago. Treatment in the past included diet control, insulin standardization, vitamins K and C, and testosterone and various forms of medication for the arthritis. A hypophysectomy had been recommended by another physician. Examination revealed numerous exudates, punctate and paracentral hemorrhages, neovascularization, mesoblastic fibrous proliferation into the vitreous originating from the area of the disc, vasculitis and scleroses in O.U. Her corrected vision was: R.E., 20/50-, L.E., 20/400. Visualization was not good in either eye. Except for some cortical lens changes, the remainder of the examination was non-contributory. Medication for the year following examination, regulated and administered by her physician, was as follows: a combination containing per tablet ergotamine tartrate 0.3 mg., total levorotary alkaloids of belladonna 0.1 mg., and phenobarbital 20 mg. 1 tablet q.i.d., meprobamate 400 mg. 1 tablet q.i.d., chlorothiazide 0.50 mg./day, KCl 1 gm./day, ethinyl estradiol 0.05 mg./day, insulin 30 US NPH plus 5 US PZI, a combination containing per capsule hesperidin complex 100 mg. and vitamin C 100 mg. 3 capsules q.i.d., atheromatosis product 2 capsules q.i.d., Orenzyme 2 tablets q.i.d., vitamin K 5 mg./day, and therapeutic dosages of vitamin B_{12} I.M. daily. On two occasions in the past, steroid therapy had been tried and discontinued because her diabetic status worsened and there was increased water retention.

Eleven months later the patient was again seen in consultation. The condition of the fundi was vastly improved and the retinitis was in a stage of remission. Her vision was correctible to: R.E., 20/20-, L.E., 20/15-. A staff ophthalmologist had seen her shortly before my examination and had noted that her retinopathy was adequately controlled.

Case 2

A physician of 42 presented himself for examination and treatment. Some ten days previously he had an attack of herpes labialis which appeared to

respond to his own treatment. Suddenly his left eye became red, sensitive to light, painful, and there was epiphora and blurring of vision. Examination revealed gross peri-corneal injection, a constricted and irregular pupil, dendritic ulcers and intrastromal disciform opacities. There were cells and a flare present in the anterior chamber. The visual acuity was 20/200, the tension normal. He was placed on 1% atropine and 10% neosynephrine drops t.i.d., topical and systemic antibiotics, Orenzyme tablet 2 stat and tablets 1 q. 4 h. and compresses. Chemical cautery of the corneal lesions was performed later. Within a week his acuity returned to 20/20+, and the other clinical findings were similarly improved.

Case 3

A woman of 40 suffered a traumatic injury with loss of vision in the left eye at age 8 years. Recently the eye had become painful and injected intermittently. Examination revealed a phthisis bulbi oculi and scleritis of the left eye. It was decided that the eye should be enucleated. She was placed on Orenzyme tablets 1 q.i.d. two days before and three days after surgery. Enzymatic and antibiotic ointments were applied topically after the eye was removed. The dressing was changed on the second day. No discoloration or bleeding could be seen and edema was at an absolute minimum. Unusually early prosthesis instillation was possible.

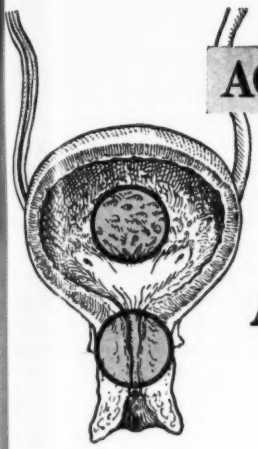
Case 4

A man of 38 sought consultation complaining of a rather sudden loss of vision in the left eye. No history of trauma or unusual circumstance could be elicited. Fundus examination revealed a greyish elevation of the macular area surrounded by hemorrhage. Some vitreous haze was present too. Visual acuity in the affected eye was less than 20/400. A diagnosis of Junius-Kuhnt disease was made. The right eye was normal. The patient was placed on Orenzyme tablets 2 q.i.d., hesperidin and vitamin C (100 mg. of each) capsules 2 q.i.d., and a mydriatic. In two weeks much of the heme had reabsorbed, macular elevation had subsided to some extent, and the vitreous was clear. Visual acuity some three months later is 20/60 with correction.

Case 5

A man of 29 gave a history of a long-standing chorioretinitis with several exacerbations and remissions. Detailed examination by a private physician and at a veterans' administration hospital failed to contribute to the etiology of the disease. Past treatment included fever therapy and steroid administration, a series of O.T. injections, topical and systemic antibiotics, and mydriasis. The Sabin and Feldman dye test was reported negative, but the toxoplasmin skin test was positive.

Examination revealed an active chorioretinitic lesion about 2½ disc diameters in size in the macular region of the left eye. Visual acuity was less than 20/200. The patient was placed on combined steroid and enzyme therapy, but it did not alter the course of the disease. Pyrimethamine and sulfa with bicarbonate tablets were substituted for the steroid. Soon the lesion began to respond. The blood picture was watched daily. About the time the white count changed and subjective symptoms appeared, the lesion was becoming pale and settled. Some pigmentary deposition about the area was noted. He was maintained on the enzyme tablets t.i.d. thereafter. The best recorded vision in the affected eye was 20/60+. Some eight months later (this was the longest interim he had experienced free of exacerbation) another active episode occurred. Pyrimethamine and sulfa were again added and the enzyme dosage was again increased to tablets 2 q.i.d. The flareup did not last as long, nor was it as severe, as the previous attack. He has been asymptomatic since this time, some nine months later. Although the enzyme



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did not of itself control the acute stage of the chorioretinitis, it was felt that it modified the active process with regard to its duration and extent and extended the length of remission.

Summary

An orally administered preparation of trypsin containing 20 mg. of the active constituent per tablet has anti-inflammatory activity and a wide margin of safety. No untoward local or systemic reactions due to this enzyme were noted in the present study of 72 cases. It is of value as an adjuvant in combating attendant inflammation and edema due to traumatic injury and surgery.

Its adjuvant use in uveal tract disease and in retinopathies is not conclusive and must be evaluated under more rigid controls. Trypsin should be considered as a form of therapy in cases where there is steroid resistance or other contraindication in protracted inflammations.◀

Management of Benign Strictures of the Bile Duct

There is great hazard to life from biliary stricture, great difficulty of surgical repair and great tendency to recurrence. In 365 (73%) of 501 patients the cause of the extrahepatic biliary obstruction could not be determined. So far as is known, biliary stricture followed cholecystectomy carried out without incident. In 136 (27%) of the 501 patients, the conditions leading to the formation of biliary stricture are known. A ductal injury was recorded by the surgeon in only 70 cases. In eight, no injury was reported, but ligatures were found around the common bile duct at the time of repair. When dissecting the cystic artery the surgeon must be alert for the right hepatic artery.

Leading the list of causes of the 39 postoperative deaths in this series is hepatorenal failure with or without hemorrhage, this occurring in about half the fatal cases. Too frequently hepatic function deteriorates after stricture repair despite rigid preoperative preparation, excellent oxygenation during the procedure, and postoperative intensive protection of liver function. The cause is obscure. Treatment of hepatic failure includes intravenous infusion of glucose in water 10% supplementary vitamin B, parenteral administration of vitamin K, and diet high in calories but limited in fat and protein. Major hemorrhage without hepatic or renal failure was the cause of death in 25% of these 39 cases.

Cattell, R. B., & Braasch, J. W., *New England J. Med.*, 261:929-933,1959.

The Use of Intravenous Estrogens to Control Pulmonary and Other Bleeding

H. SHUBIN, M.D., C. A. HEIKEN, M.D.,
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►*Among 38 patients having pulmonary tuberculosis, lung abcess, or bronchiectasis, and 24 with postsurgical bleeding, peptic ulcer, epistaxis, or menorrhagia, intravenous estrogens proved to be a favorable means of controlling hemorrhage because of its ease of administration and nontoxicity.*◄

Hemorrhage has been a fear of both patient and physician for centuries. The bleeding of the tuberculous patient was, up to 15 years ago, a major medical problem, and remains today a problem of importance. Up to now there has been no method that provided simple and effective control of pulmonary bleeding.

In 1955 it was decided to administer intravenous estrogens* to patients with pulmonary hemorrhage. There were no reports on its use in pulmonary bleeding, although it had been used successfully in epistaxis, and in uterine, post-tonsillectomy and gastrointestinal bleeding.[1-4]

*Premarin Intravenous®, Ayerst Laboratories, New York.

Procedure

Therapy was evaluated in a pilot series of 14 patients. Results were encouraging and a larger series, with controls, was undertaken. To date, 38 patients have received intravenous estrogens for the control of pulmonary hemorrhage. Only patients having free bleeding of more than 100 cc. were treated. Patients with only streaking were managed with bed rest. Thirty-three patients had pulmonary tuberculosis, 2 had lung abscess, and 3 had extensive bronchiectasis.

Five patients with pulmonary tuberculosis served as controls, either receiving conservative therapy such as bed rest, ice bags,

1. Greenblatt, R. B., & Barfield, W. E., *J. Clin. Endocrinol.*, 11:821,1951.
2. Reich, W. J., et al., *J.A.M.A.*, 152:1679, 1953.
3. Jacobson, P. A., *West. J. Surg.*, 63:711, 1955.
4. Menger, H. C., *J.A.M.A.*, 159:546,1955.

and/or vitamin K, carbazochrome salicylate, or intravenous pituitrin. Two were given artificial pneumoperitoneum.

Results

Hemorrhage was controlled within 30 minutes in 30 of the 38 patients who were given intravenous estrogens. The other 8 patients continued bleeding and were given another injection within one hour. Six of these ceased bleeding within an hour after this second injection. Two patients died of hemorrhage. Autopsy on one of these revealed a large, necrotic lung abscess with ulcerated large blood vessels.

In two of the 5 control patients hemorrhage stopped within 12 hours. One had received pituitrin intravenously and another artificial pneumoperitoneum. The third patient gradually stopped bleeding after 24 hours. The last 2 patients continued moderate bleeding and were given intravenous estrogens after 24 hours. Hemorrhage was controlled within two hours.

Two Dozen More Treated

During the course of the study, an additional 24 patients with bleeding from sites other than the lungs were treated with intravenous estrogens. Six had severe epistaxis, 3 moderate bleeding after dental extraction, 3 post-tonsillectomy bleeding, 7 bleeding peptic ulcer, and 5 menorrhagia. Results were excellent in this group, also, with control of bleeding within two hours in 20 of the 24 patients. One patient with epistaxis and severe hypertension continued to bleed for eight hours. He was given only one injection as it was considered advisable that the bleeding continue for a while, to relieve the hypertension. One of the patients with peptic ulcer continued to bleed and at operation it was found that the ulcer had perforated into the pancreas. The third patient had a uterine fibroid with an ulcerating carcinoma, which required surgery.

Conclusion

The absence in all patients of side effects, untoward reactions or toxicity, as well as the simplicity of administration, was impressive. It appears that in the practice of internal medicine, intravenous estrogens served as a non-toxic, easily administered agent for rapid and effective control of hemorrhage.◀

case report

Gangrene of Forearm Following Intramuscular Injection of Chlorpromazine

R. J. H. HODGES, D.A., *Portsmouth, England*

►*A patient undergoing treatment for decubitus ulceration following extensive third-degree burns was given chlorpromazine. Gangrene developed and despite heroic measures the patient later died. It appears that periarterial puncture caused the thrombosis which was unrelieved by surgery or heparinization.*◄

A woman of 52 with a history of psychotic instability and having third degree burns over 35% of her total body surface from the waist downwards, relapsed into acute mania after skin-grafting. During psychotherapy the burn areas were treated in enveloping plaster and re-dressed as necessary under light general anesthesia. Sepsis and decubitus ulceration took place under the plaster jacket, resulting in toxemia and signs of renal damage. Blood transfusions and strenuous general measures were necessary to maintain her general condition. After five months the patient was alert and sensible, but her physical state had slowly depreciated and she had not tolerated repeated anesthesia well.

On occasion of the second dressing 50 mg. chlorpromazine was given intramuscularly by a trained staff nurse into the anterior aspect of the right biceps area. No complaint of pain or discomfort was made at the time, but 20 minutes later the patient remarked that her arm felt dead. Examination showed it to be flaccid, cold, and white. The brachial artery was pulsating in the upper arm, but from the site of injection downwards no circulation could be detected. From 1½ inches above the elbow-joint to the finger-tips the limb appeared to be exsanguinated. Although procaine 5% was immediately infiltrated around the brachial artery at the injection level, and 25 mg. tolazoline administered intramuscularly, neither measure had any obvious effect.

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About 2½ hours later a stellate ganglion and brachial plexus block was performed using 1% lignocaine, this followed after 15 minutes by signs of Horner's syndrome, but by no alteration in the appearance of the arm. A few minutes later 40 mg. papaverine in 20 ml. of water was injected into the subclavian artery, after which there appeared to be a slight flushing of the skin for an inch or more below the previous line of exsanguination. Immediately after this procedure 15,000 units heparin was given intravenously.

Surgical exploration (anesthesia for which was thiopentone, cyclopropane, nitrous oxide and oxygen) undertaken eight hours from the time of the original injection revealed some periarterial discoloration and hematoma formation, but no evidence that the artery had been punctured. From the point of puncture downward the vessel was contracted and immobile, and no blood could be aspirated from it. A 2% solution of papaverine was applied locally and 40 mg. of the drug in 20 ml. of water injected into the artery at its lowermost normal point. These measures had no visible effect. Arteriotomy and arteriectomy were considered inadvisable.

Post-operatively, continuous heparinization was maintained and vasodilation encouraged by intramuscular administration of tolazoline and by contralateral limb-heating. Support and gentle passive exercises were applied to the affected limb. In a few days there was a slight regression of the exsanguinated area on the radial side of the arm. Mottled bluish patches appeared around the surgical wound in the upper arm and spread into the forearm, particularly on the ventral aspect. The remainder of the forearm and hand remained bloodless, flaccid, and cold. Dry mummification took place in the finger-tips. A line of separation eventually appeared, medially just below, and latterly just above, the elbow-joint. By the fifth day it was obvious that amputation of the forearm was inevitable, but in view of the patient's gradually worsening condition conservative treatment was continued. The patient died in uremic coma two weeks after the injection of chlorpromazine.

At necropsy gangrene of the right hand, forearm, and elbow was confirmed, the brachial artery being thrombosed from the mid-upper arm downward. The artery was occluded by an unorganized red thrombus, there was no evidence of intimal proliferation, and the elastic laminae and media appeared normal. The vessel was incompletely surrounded by an organizing hema-

toma involving the adventitia. Pathologic condition of the arm was considered to be one of several associated causes of death, the primary cause being septicemia after burns.

Chlorpromazine causes pain and irritation after injection, along with an apparent inflammatory reaction. Thrombophlebitis, sterile abscess formation, and sloughing may occur occasionally, all necessitating skin-grafting. In the case reported the drug produced intense arterial spasm. Since the patient did not complain of any symptoms at the time of injection, and at operation there was no local evidence of arterial puncture, the assumption remains that the periarterial injection caused an intense local irritation and an intractable peripheral arteriolar spasm. In another case a similar irritant effect on an adjacent artery after an inadvertent perivenous injection of other phenothiazine derivatives, resulted in gangrene of a limb. The appearance of the arm and the absence of edema in the present case suggested that the circulation was completely arrested in the forearm and that the main digital arteries became thrombosed within a very short time.

The only beneficial effect appeared to follow the early intra-arterial injection of papaverine. General anesthesia of the type used is said to increase the peripheral circulation by 64%, but neither this nor the local operative measures applied resulted in any measurable effect in the limb.◀

Brit. M.J., 2:918-919,1959.

Occlusive Arterial Disease

The effect of nylidrine HCl (Arlidin) on blood flow response to exercise was tested plethysmographically in 3 healthy subjects and in 7 patients with nongangrenous occlusive arterial disease of the lower extremities. In response to exercise of the lower extremity after 7 mg. intravenous nylidrine, 9 of the 10 showed blood flow increases averaging 112.0% (as compared to 65.5% after exercise alone) with little or no change in surface temperature. Increases in flow attributable to nylidrine, i.e., over and above those caused by exercise alone, ranged from 18 to 25% in normal subjects and from 20 to 147% in those with occlusive disease.

Nylidrine appears to act primarily on the vasculature of skeletal muscle, enhancing capacity of these vessels to dilate in response to exercise without causing skin vasoconstriction.

de Crinis K., et al., *Proc. Soc. Exp. Biol. & Med.*, 102:29-31,1959.

Idiopathic Pulmonary Hemorrhage in Pregnancy

VICTOR GUREWICH, M.D., and
M. A. THOMAS, M.D., *Tampa, Florida*

►*Respiratory complications during the third trimester of pregnancy were noted in a woman who had had no previous serious complaints. Pregnancy was terminated by the delivery of a premature, yet healthy infant. This history indicates that steroids may be considered in early pulmonary hemosiderosis.*◄

A gravida 2, para 1 of 22, seven months pregant, had her first prenatal examination five months previously, this showing hb. 12.9 gm./100 ml., hematocrit 30%. Routine chest x-ray three months later was normal. A pregnancy one year earlier was without complication. Nausea and vomiting in the first trimester and failure to gain weight were the only complaints up to the time of the present illness.

On admission hb. was 4.8 gm. Fatigue, slight exertional dyspnea and a nonproductive cough for three weeks were the only complaints. Obvious pallor was the only abnormal sign. Test for occult blood in the stool was negative, becoming positive two days later. After receiving 2500 ml. of whole blood, the patient was discharged, at which time hb. was 9.6 gm., hematocrit 26%. Three days later she returned, the chief complaint being shortness of breath. In the interval, cough had become much more severe. She was weak, orthopneic (requiring 2 pillows) and dyspneic at rest. The only medication had been vitamins containing iron and calcium. Clinical picture revealed a gravely ill woman in obvious respiratory distress, with marked cyanosis, distended neck veins, and systolic gallop rhythm. The chest was clear to percussion and auscultation, abdomen soft and nontender, uterus palpable 2 cm. above the umbilicus. Temperature was 102.4, pulse 140 and regular, respiration 45, blood pressure 120/75. X-ray study of the chest

showed a massive, mottled infiltration of both lung fields tending to spare the apexes and the costophrenic sulci. The cardiac contour was normal. Hb. was 6.7 gm., hematocrit 17%, white cell count 7400 (54% neutrophils, 43% lymphocytes, 2% monocytes, and 1% eosinophils). Sedimentation rate was 69 mm. per hour, platelets normal, reticulocytes 4.8%. Sputum and throat cultures showed a few colonies of Str. pyogenes. Blood and urine cultures were negative. Aspiration disclosed a normal, active bone marrow, ECG normal.

Hospital course initially was one of continued respiratory distress, marked, immediate cyanosis on removal of the oxygen mask and maximum temperature of 104°. She once coughed up a small amount of bloody sputum. Treatment consisted of oxygen, bed rest, transfusions with packed cells, intramuscular injections of iron (Imferon), tetracycline, 500 mg. orally every 6 hours, crystalline penicillin, 1,000,000 units every four hours, and streyptomycin, 0.5 gm. every 12 hours. Digitalization and 2 ml. of mercaptomerin failed to produce a diuresis or clinical improvement. On the third hospital day she went into labor, and a premature but active, healthy female infant of 4 lbs. was delivered. Baby's hb. was 20 mg. per 100 ml. No more than 100 ml. of blood was lost. On the fifth hospital day a presumptive diagnosis of idiopathic pulmonary hemosiderosis was made and prednisone, 10 mg. 4 times a day, and 40 units of ACTH gel every third or fourth day were given. By the sixth hospital day patient was afebrile, cough, cyanosis and dyspnea no longer being evident. X-ray study revealed early resolution of the infiltrate. Steroid therapy was maintained at gradually reduced doses for a period of four weeks. On the tenth day, a lung biopsy specimen was taken through a thoracotomy incision in the fourth right intercostal space. Chest x-ray on this day showed almost complete resolution, with residual stippled and reticular markings. Patient was discharged 10 days later. Follow-up over a period of 12 months has shown the patient to be asymptomatic, her present hb. being 12-14 gm., x-ray films clear. Biopsy specimen revealed focal alveolar hemorrhage, slight edema and few alveolar macrophages containing hemosiderin pigment. Many of the alveolar walls were thickened, portions being composed of an eosinophilic hyaline material.

This diagnosis should be considered in unexplained anemia associated with a diffuse pulmonary infiltration.◄

New England J. Med., 261:1154-1159,1959.

Fractures in Children

DONALD S. MILLER, M.D., *Chicago, Illinois*

▶*Many fractures among children are amenable to immobilization by an elastic bandage. Fractures near the wrist often present difficulties requiring a high degree of orthopedic skill. Bryant's traction is treatment of choice for femur fractures among young children, but a Thomas splint is better for those who are older.*◀

Most fractures of the forearm (including the wrist) are of the simple cortical green-stick type or the torus type. They have minimal angulation, are not displaced, and require only simple measures of temporary immobilization. Application of an elastic bandage or an extremely lightweight cast are generally suitable, but these must not be tight. Fractures of the upper third of the forearm require more supination than do those of the middle or lower third, which require more pronation.

Fracture of the Lower Forearm

One of the commonest and most difficult fractures to treat is that of the lower sixth of the forearm in which there is dorsal displacement of the distal short fragments. An overriding deformity requires some technical skill in correcting. The general plan is the application of a well padded forearm cast, preferably extending above the elbow, which is worn for six to eight weeks. The usual way in which injuries to the elbow are incurred is by sudden hyperextension of an upper extremity. Although good alignment results in the usual supracondylar fracture of the elbow, an osteotomy of the humerus is occasionally required.

Fracture of the Upper Forearm

Less common, but more serious and sometimes disastrous, is fracture of the upper sixth of the ulna with the head of the radius displaced. This requires reduction of the fragments by hyperextension and traction in order to achieve integrity of the elbow joint. Extension of the elbow followed by careful flexion and firm pressure over the head of the radius are essential, the sur-

geon's thumb acting as a lever. The patient's forearm is pronated before application of a light padded case. Pressure must not be made by tight cases or bandages on the arterial inflow or venous return. Any spicule of bone which can cut into an artery must be watched for. Casts should be well padded and replaced, if necessary in a few days. X-ray follow-up studies are indicated to detect any displacement.

Fractures of the Clavicle and Femur

Fractures of the clavicle are treated by immobilization of the shoulder for two to six weeks, depending on severity, displacement, and soft tissue involvement. For the simple, cortical, mildly deformed fracture, adhesive tape retention (unless the skin is sensitive to adhesive tape) or a sling is sufficient. An active child may require lightweight spica casts including both sternoclavicular joints, applied comfortably, with the shoulders immobilized properly. A spica cast seems to serve better than the figure-of-eight bandage.

Fractures of the femur in patients under three or four years are best treated by Bryant's traction, with extreme care in the application of the moleskin and bandages, and peripheral circulation carefully watched. Both extremities should be carefully padded, and moleskin tape or foam rubber strips applied without restriction. Tight elastic bandages are contraindicated. The color of the extremities, injured and uninjured, must be diligently and continuously observed. When circulation is affected, traction must be removed at once.

For children of six to 12 years traction by a Thomas splint or Russell traction is best. The shaft of the femur need not be completely reduced. Side-to-side bone contact is adequate, but rotation and angulation must be prevented. Duration of traction is longer than for younger children and more weight is necessary.

Other Fractures

Compression injuries of the foot and of the hand make a special group. Because of serious hemorrhages in these areas and pressure on lymphatic vessels, local deep scarring and superficial tissue necrosis and amputation may ensue. Complicated joint fractures, though skillfully treated, frequently result in some loss of mobility, shortening or deformity. Fractures of the outer condyle through the capitellum require open reduction and fixation with pins or screws. Hyperextension injuries of the elbow joint, causing displac-

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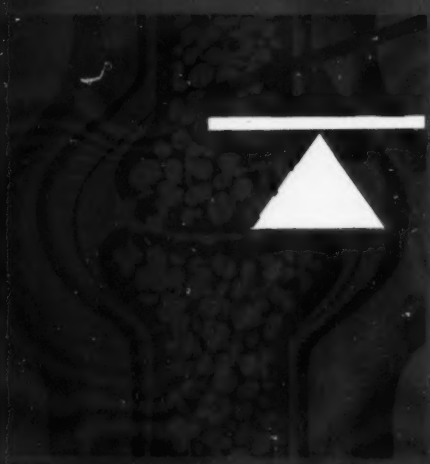


Geigy

ment of the head of the radius, can be reduced at times under general anesthesia by careful gentle pressure while the arm is extended, after first flexing the joint, and by applying pressure throughout this maneuver to the head of the radius.

In fractures through the femoral epiphysis, pin fixation may be necessary. Manipulation in extension and flexion may reduce the displaced distal short fragment, followed by traction. A pin or screw should be carefully inserted so as to avoid the growing epiphysis. If not treated properly, serious interference with function of joints and permanent crippling may result. Open reduction must be resorted to if conservative attempts at reduction fail.

Olecranon fractures with separation, patellar fractures with separation, and the rare pelvic fracture with symphysis pubis separation will probably require open reduction (as will the neck of the femur when fragments must be reduced in and about the knee joint).

The vascular supply of infants and small children may be so disturbed in fracture of a lower extremity as to produce aseptic necrosis. Neglect of compression fractures of the feet may lead to gangrene and amputation.

In the developing epiphyses of children self-correction may be anticipated after the initial reduction. Overmanipulation invites complications. It is the clinical condition of the child and his joint that should be treated, not the x-ray appearance of that joint. X-rays are taken to follow the course of angulated or rotated fractures and those causing shortening — these may not be left to time and natural repair.

Hidden fractures may be disclosed by later rather than by the immediate bilateral x-rays.

Salient points to remember are:

1. Avoid rotation and angulation.

2. Correct alignment.

3. Avoid tight bandages and pressure.

4. Be watchful of the circulation. To that end, leave the toes exposed when applying a cast in order to observe the color.

5. Surgical intervention is not necessary unless the fragments show sequestration by the primary injury or because of the myodynamics, e.g., of the olecranon or of the condyles of the elbow or knee.

For the welfare of the child and self-protection against lawsuits, a thorough and detailed history must be filed in the hospital records.◀

Minnesota Med., 42:1414-1425,1959.

Some Etiologic Problems in Mental Deficiency

J. M. BERG, M.D., and
BRIAN H. KIRMAN, M.D., *London, England*

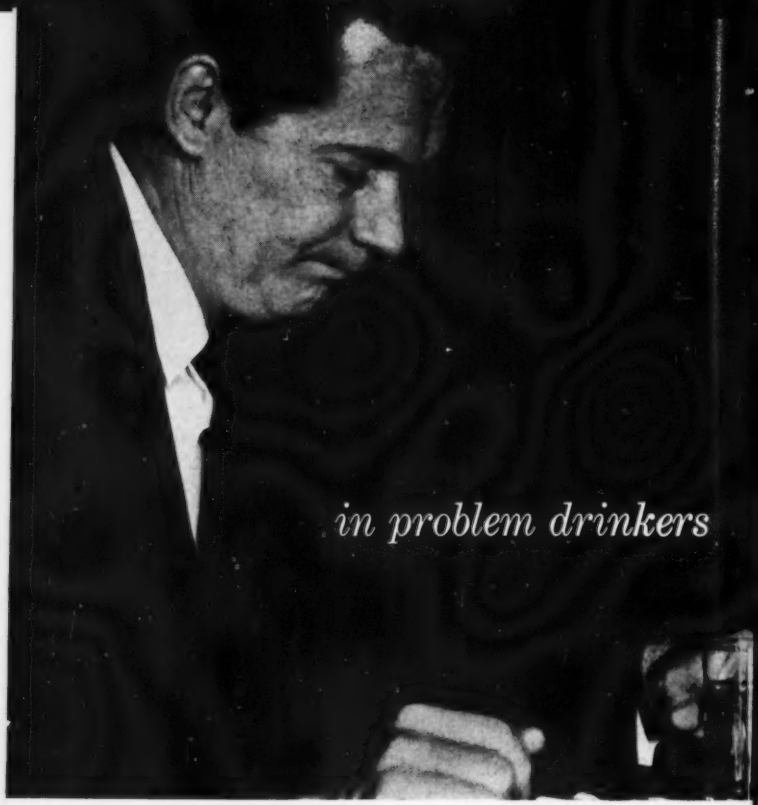
▶*Phenylketonuria, blood-group incompatibility, mongoloidism, and vitamin deficiency are some of the causes of mental deficiency in children. Studies have revealed that metabolic disturbances may reduce vitamin A uptake, resulting in mongoloidism. Similar disturbances may be a transmittable hereditary factor.*◀

Mental deficiency may conveniently be considered in two groups—minor (high-grade) and severe (low-grade). Some cases of mental defect have been regarded as pathologic, some as subcultural. This thesis assumes that some defectives are such because of pathologic lesions, others because of biologic variation.

Definitions based on IQ are of little value, while those based on legal recognition or ascertainment as mental defectives are of even less value. It should not be assumed that gross pathologic lesions are encountered only in idiots and imbeciles. All the diseases and factors contributing to gross mental deficiency may operate in a form producing minor degrees of mental defect.

Theories of Etiology

Phenylketonuria may be taken as an example of a genetically determined form of specified defect, the effect of which on mentality may range from idiocy to average intelligence. Damage due to rhesus blood-group incompatibility illustrates a similar phenomenon produced by an environmental factor. It is possible in nearly all idiots and imbeciles to find changes in the brain after death. Marked disturbance of function may occur with little obvious brain abnormality. Mongolism remains by far the biggest single clinical group among mental defectives. Although there is little clue to its etiology, it is possible to construct a hypothesis which will cover the fact that quite young mothers may have children with



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mongolism and that the older mother may have an affected child followed by a normal one. It may also be assumed that the predisposition to give birth to such children lies in difficulty in dealing with a metabolite which is particularly important at the organogenetic stage of development. If, for example, the abnormality were to lie in a difficulty on the part of the mother to absorb vitamin A (known to be essential for organogenesis), then this difficulty might well be exaggerated by increasing age, and might be made worse in one pregnancy rather than another by external circumstances. Illness or poor diet would increase the effect of such a deficiency.

No case has been recorded in which only one of monovular twins was affected, while there are many recorded instances of only one of binovular twins being abnormal. If, therefore, the above hypothesis is to cover the facts, it must be extended to assume that there is a predisposition on the part of the mother to have children with mongolism, and that this predisposition may be inherited so that the fetus likewise is predisposed to be a "mongol" in certain cases but not in others. It may be that the fetus has the same difficulty in the uptake of vitamin A which was suggested in the case of the mother. The combined effect of the maternal and fetal abnormality would then be a frank case of mongolism if external conditions such as advanced maternal age were also unpropitious.

Specific metabolic peculiarities in mongolism have been difficult to demonstrate, though abnormalities in leucocytes, proteins, cholesterol, phospholipids, and calcium are now firmly established. Recent work suggests that children with mongolism have a reduced capacity for the uptake of vitamin A. These workers propose that the blood of pregnant women should be examined for the vitamin-A content.

General Hypothesis

Although two-thirds of all idiots and imbeciles present no substantial clue as to etiology, nearly all of these cases have some gross encephalopathy. It seems likely that in the course of time further specific syndromes will be discovered which will account for some fraction of this total, and that some of these will prove to be inborn errors of metabolism transmissible on classical Mendelian lines. However, it seems unlikely that more than a small fraction will be accounted for in this way. Attention must also be paid to the fetal environment and to the maternal environment in the case

of mongolism. Little is known about the optimum maternal environment for the development of the fetus, however, the nutrition, health, and well-being of the mother, during and before the pregnancy, is of great importance in connection with the subsequent mental development of the child.

Review of Cases

Of 44 educationally subnormal children, 32 (73%) had clinical abnormalities which could at least partially account for, or be related to, their mental retardation. In another 12 high-grade patients who came to necropsy, only three had no gross pathological lesions in the brain. Nearly all low-grade mental defectives show brain abnormalities at necropsy. The cause of these is elucidated in a small minority only.

In 200 consecutive hospital admissions of low-grade cases, a known cause was operable in 19 (9.5%) and a probable cause in another eight (4%). Other factors were implicated in 111 (55.5%) and none in the remaining 62 (31%). Of these 200 cases 46 (23%) were mongoliod, their condition tentatively attributed to a biochemical error in the mother becoming more manifest with increasing age and leading to faulty organogenesis in a predisposed fetus. Of the remaining 154, 122 (79%) had gross physical signs.◀

Brit. M.J., 2:848-852,1959.

Puerperal Cardiomyopathy

Reports of cases with strikingly similar histories and clinical courses have been made under such titles as "idiopathic myocardial degeneration associated with pregnancy, and especially the puerperium," "toxic postpartal heart disease," "post-partum myocardosis," and "myocardial failure in last trimester of pregnancy and the puerperium." The syndrome consists of congestive heart failure occurring in the last trimester of pregnancy and the puerperium with no previous history of cardiovascular disease. Features are sinus tachycardia, small pulse volume, triple rhythm, precordial systolic murmur, a loud second sound in the pulmonary area, profuse sweating, emboli, and cardiographic evidences of myocardial disease. To date, 102 cases have been reported in the United States and Canada and only three in Great Britain. No satisfactory cause for the degeneration has been discovered.

Rosen, S. M., *Brit. M.J.*, 2:5-9,1959.

Unrecognized Foreign Bodies in the Air and Food Passages

PAUL G. BUNKER, M.D., *Aberdeen, South Dakota*

▶*Seven case histories are presented to illustrate the point that foreign bodies may sometimes lodge unobtrusively in the esophagus and the airway and later present respiratory symptoms which may offer no clue concerning the cause. Some points of procedure are offered to reduce this possibility.*◀

Unrecognized foreign bodies in the air and food passages are more common than is generally realized and should be considered in the diagnosis of any unexplained respiratory difficulty or dysphagia. Some secondary infections improve under antibiotic and chemotherapy, only to flare up again when treatment is discontinued. For diagnosis, x-rays at 1/60th of a second are essential to show the foreign body and secondary changes and anatomical variations which might complicate the endoscopic picture. Illustrative cases follow:

Case 1

A boy of 9 gave a history of foul breath, unilateral nasal discharge from the right side and frequent upper respiratory infections for two years previously. He was underdeveloped for his age. Tonsill- and adenoidectomy, special medications, and special diets had all been tried at various times. X-ray picture of the sinuses showed a large safety pin in the right nasal cavity. Removal gave complete relief of all symptoms, the child gaining 10 pounds in six weeks.

Case 2

A baby of 17 months had a penny in her esophagus and dysphagia for over one year. Several doctors had been consulted and various medications given. The last took an x-ray and found the coin in the mid-esophagus. Removal of the coin was uneventful, but a stricture had developed and a bolus of food had to be removed several times before the stricture dilated. The child has been asymptomatic for several years.

Case 3

A woman of 40 gave a history of a chronic cough with dyspnea, low-grade fever and hemoptosis since age 5. She had gone through 4 pregnancies uneventfully. Tuberculosis had been suspected but never proven. She finally consulted a doctor who made an x-ray showing the pointed shaft and ring of a safety pin in the right main bronchus. The lung was atelectatic, the right chest much smaller than the left, the thoracic spine curved. Re-

moval of the pin was not difficult, resulting in subsidance of hemoptysis and pronounced reduction of cough. She has been reasonably well in the 18 years since removal of the pin.

CASE 4

A baby of 11 months had marked dysphagia, salivation and dyspnea in the prone position for 3½ months and later, huskiness and swelling in the left side of the neck. Treatment with antibiotics by several doctors was not helpful. X-rays were finally taken, showing an open safety pin in the hypopharynx The pin removed, infection promptly subsided under antibiotic treatment.

CASE 5

A baby of 8½ months had dysphagia for 6 months along with episodes of acute respiratory distress and high fever. The infection subsided under antibiotic therapy and recurred on discontinuance. Fluoroscopy revealed presence of a button. The child made an uncomplicated recovery after the button was removed

CASE 6

A baby of 25 months had wheeze for 2½ months and was referred for allergy tests. Through the bronchoscope a watermelon seed was found and removed from the right main bronchus. Recovery was uneventful.

CASE 7

A woman of 52 had a history of high fever, chills and severe back ache of 5 days' duration. She swallowed comfortably, and gave no history of choking on a foreign body. X-rays showed evidence of mediastinitis. After several days of treatment to control infection, a large triangular piece of bone was removed with forceps from the lower third of the esophagus. Subsequent antibiotic therapy resulted in complete recovery.

Treatment "Do's and Don'ts"

1. Use x-ray in any unexplained case of dyspnea, wheeze or dysphagia.

2. Use a duplicate of the foreign body for selecting the best forceps for removal of the original.

3. Be careful of loose teeth when inserting a mouth gag.

4. Make general examination before endoscopy for aneurism, high blood pressure or other cardiovascular disease, and spinal deformity.

5. Do not reach into the mouth with the fingers.

6. Do not hold the patient up by the heels and slap his back in an effort to remove a foreign body from the trachea, as this may cause asphyxia due to impingement of the foreign body against the glottis.

7. Do not pass instruments blindly into the esophagus.

8. Remove foreign bodies as soon as possible. Although only 2 to 4% of all foreign bodies in the tracheo-bronchial tree are coughed out spontaneously, 99% can be removed by bronchoscopy.

9. No morphine.

10. Do not give dry bread or crackers to a patient with a foreign body in the esophagus, since increased secretion may greatly interfere with esophagoscopy.

11. Allow the patient to assume a comfortable position.

South Dakota J. Med. & Pharm., 12:473-48[illegible] 1959.

Treatment of Malignant Pelvic Tumors by Extracorporeal Perfusion with Chemotherapeutic Agents

W. GERALD AUSTEN, M.D., ANTHONY P. MONACO, M.D., GEORGE S. RICHARDSON, M.D., WILLIAM H. BAKER, M.D., ROBERT S. SHAW, M.D., and JOHN W. RAKER, M.D., *Boston, Massachusetts*

▶*By isolating the circulation system surrounding a tumorous region, therapeutic agents may be infused which might otherwise be toxic to the entire system. Pelvic carcinomas present special problems of isolation, which are not difficult when proper pressure-flow relations are maintained with the oxygenator.*◀

An important limitation to intravenous use of nitrogen mustard and allied compounds has been the toxicity of these drugs to the normal tissues of the gastrointestinal tract and hematopoietic system. Doses within the limits of systemic tolerance are often without tumorocidal effect, and larger doses may cause systemic toxicity hazardous to life. Although intra-arterial administration of nitrogen mustard produces high local tumorocidal levels it does not entirely eliminate systemic toxicity, and frequently causes severe local reaction and vascular thrombosis.

By isolating the circulation of a region bearing a tumor and perfusing it by use of an extracorporeal circuit, the twofold advantage of minimizing systemic toxicity and presenting high levels of alkylating agent to the tumor and its immediate surroundings may be achieved. An oxygenator is incorporated into the perfusion circuit to gain the possible advantage of increasing the effect of the radiomimetic agents in view of evidence that radiation is more effective at high tissue oxygen tensions.

Application of this technique to regional perfusion of the lower extremity makes vascular occlusion in this area so complete that the dose of chemotherapeutic agent permissible is limited by local tissue tolerance rather

than by systemic toxicity. Isolation of the pelvic vessels is less complete and less reliable, so that the danger of systemic toxicity incident to the mixing of the perfusate with the general circulation limits the dose of drug that can be given.

Vascular Isolation of the Pelvis

This is achieved by occlusion of the aorta and vena cava by suitable non-crushing vascular clamps, and of the femoral vessels in both lower extremities by pneumatic cuffs inflated around the upper thighs. The femoral vessels are exposed in the leg proximal to the pneumatic cuff, the perfusion is carried out through No. 14 plastic cannulas inserted into the artery and vein and threaded proximally into the external iliac vessels. Occlusion of the aorta is accomplished above the bifurcation but below the origin of the inferior mesenteric artery to exclude the bowel from the perfusion. For exposure of the aorta and vena cava the retroperitoneal approach is preferred since it permits easy access to the aorta and vena cava, is safer (particularly when the abdominal wall is involved with cancer or has adherent small bowel beneath it), and decreases postoperative ileus by avoiding entrance into the peritoneal cavity.

Extracorporeal Circuit

The one employed is a modification of the Kay-Cross Rotating Disc Oxygenator utilizing a single sigmamotor pump with gravity venous return. The oxygenator is primed with 1,000 ml. of blood removed from the patient via the venous catheter with simultaneous replacement by transfusion into the antecubital vein. Perfusate temperature near 37°C. is maintained by heating the oxygenator.

Pressure-Flow Relations

The pelvic-perfusion pressure and the systemic pressure are monitored by indwelling arterial needles in the opposite femoral artery and left radial artery, respectively, pressure transducers and recording equipment being used. In general pelvic perfusion is done at a pressure of 70 mm. Hg and flow rates of 500 ml. per minute, mixing with the general circulation being decreased by minimizing flow through uncollateral vessels.

Mixing with the General Circulation

This is greater and less predictable during a pelvic than during a lower-extremity perfusion. Even with best occlusion many collateral channels are still open. Furthermore, pelvic tumors may have obstructed nor

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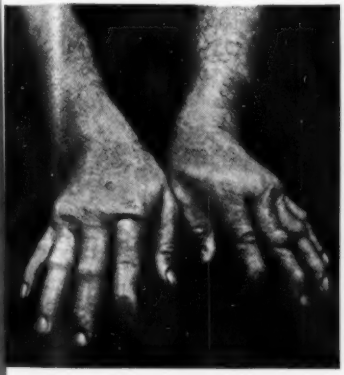

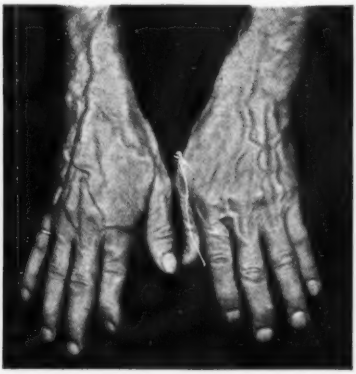

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mal channels, causing development of additional collaterals. To determine the extent of mixing with the general circulation, serial samples of blood are drawn from the perfusate and general circulations and determination of radioactivity in the general circulation done at each sampling.

In contrast to perfusion of the lower extremity, in which vascular isolation can be nearly complete, perfusion of the pelvis produces enough loss of perfusate to the general circulation that the dose of chemotherapeutic agent must be limited by the risk of systemic toxicity.

In applying perfusion technique to the pelvis, isolation of the pelvic vessels via the retroperitoneal approach seems to be easier and safer, and it may bring about a smoother convalescence. Perfusing the pelvis with the patient's own blood maintained at physiologic temperature and pH will avoid peritoneal reactions associated with the use of bank (ACD) blood. It is possible that pelvic perfusion with nitrogen mustard compounds can be combined with radiation therapy for increased effectiveness.

Maintenance of the perfusion pressure at a lower level than the systemic pressure minimizes the loss of drug to the general circulation.

The extent of mixing of the perfusate with the general circulation in pelvic perfusion is not accurately predictable. Monitoring the rate of mixing of the two circulations during perfusion affords the best means of administering the maximal amount of agent with the minimal risk of systemic toxicity.

In the usual pelvic perfusion the rate of mixing is 1.5% per minute. Under such circumstances high doses of nitrogen mustard (1.0 mg. per kg. of body weight) may be given safely. Obstruction of pelvic veins by tumor results in increased collateral blood flow with a mixing rate of some 3% per minute, and requires reduction of the dosage of nitrogen mustard to 0.8 per kg. When occlusion of the major vessels is not complete or cannot be attempted, drug is lost to the general circulation at a rate of some 4% per minute, the permissible dose being 0.4 to 0.5 mg. per kg.

Systemic toxicity is also dependent upon the duration of action of the drug employed. With the same rate of loss of perfusate to the general circulation, a short-acting drug is better tolerated than a longer-acting agent of comparable dosage. The employment of combinations of drugs with similar effects on tumors and different systemic toxicities may produce more

damage to the tumor without increasing the hazard.

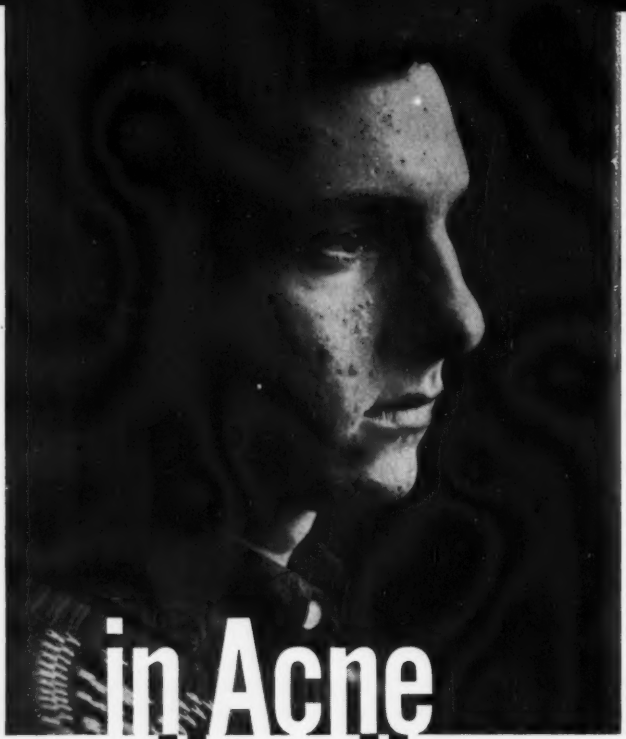
Perfusion with chemotherapeutic agents is particularly applicable to pelvic cancer, since tumors of this area frequently cause morbidity and mortality by local encroachment, rather than by distant metastases. Control of local disease may result in prolonged survival.◀

New England J. Med., 261:1037-1045,1959.

Acute Rheumatic Fever: Prednisone Therapy Complicated by Leukocytosis

This complication, though having no apparent pathologic consequence, is worth noting because a single elevated leukocyte count might be misinterpreted as evidence of activity of the rheumatic infection. Leukocytosis in the range of 16,000 to 20,000 cu./mm. was observed in 3 children aged 8 to 10 under treatment with prednisone for acute rheumatic fever. Dosage ranged from 30 to 80 mg./day. In each case the leukocytosis began within a few days after prednisone was started and ended within a few days after it was stopped. In no case were there any other signs of activity of the rheumatic process, nor could any evidence be found of any other infection.

Harris, T. N., & Vandegrift, H. N., *Pediatrics*, 25:80-84,1960.



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1. Smylie, H. G.; Webster, C. U., and Bruce, M. L.: *Brit. M. J.* 2:606, Oct. 3, 1959. 2. Hodges, F. T.: *GP* 14:86, Nov., 1956.

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Facts and Fallacies About Gonorrhea and Syphilis

WARFIELD GARSON, M.D., M.P.H.,
Chapel Hill, North Carolina

►*Even the best diagnostic measures fail to detect gonorrhea in some females. Penicillin is effective only with high serum levels and in long-acting forms. Among the newer serologic tests for syphillis are the RPCF and the TPCF 60 tests, which are inexpensive and readily available. The TPI test is readily available.*◄

Measures employed in this disease are not justifiable in the light of current knowledge. If it is assumed that the best procedure for the diagnosis of gonorrhea in women is by smears and cultures taken from appropriate sites correlated with clinical data, 25 to 50% of the cases will be missed, because the most sensitive diagnostic tool available for the diagnosis of gonorrhea in the female is the anterior urethra of a susceptible male. This disease will not be controlled as long as one of every two to four women having it cannot be detected by current laboratory procedures.

Problems of Treatment

While the organisms causing syphilis are highly susceptible to the action of penicillin, this has never been true for N. gonorrheae. It has always taken more penicillin per organism to achieve a minimal inhibitory concentration (MIC) for the gonococcus than for the treponeme. Furthermore, the gonococcus has a wide range of susceptibility to the action of penicillin, depending upon the strain. Natural isolates of the gonococcus over the past decade have indicated a continuing proportional increase in resistance to penicillin. Failures of treatment on the basis of dose or drug alone has been observed in a number of clinics. The bacteriocidal effect of penicillin on the actual strain of the gonococcus becomes observable between the fourth and fifth hour of contact of the organism with the drug,

and is usually complete by the twelfth hour. Occasionally, on a few strains tested on semi-solid media, viable organisms can be recovered through 24 hours of contact with penicillin. However, no strain has ever survived as long as 48 hours of exposure under these circumstances. These factors could not account entirely for the failure of penicillin to cure some infections, particularly in the female.

Requirements for Effective Treatment

Taking into consideration all the known factors, a working hypothesis for the treatment and management of gonorrhea consists of the following:

1. Sufficient penicillin must be given so that the units per ml. of serum will not exceed the highest known MIC for any strain of the gonococcus in this country (a serum level of 0.35 units per ml.).

2. This level must be maintained in contact with the gonococcus for at least 24, preferably 48 hours.

3. Provisions should be made in the treatment for very long-acting penicillin, since 48 hours of exposure will kill all gonococci *in vitro* but it is not known when such exposure is liable to occur *in vivo*, particularly in the female. Even more important, reinfection may quickly occur. It is possible with benzathine penicillin to obtain blood levels beyond 45 days in humans. While the exact minimum concentration of continuous penicillin that will protect a person exposed to gonorrhea is not known, it is known that giving long-acting penicillin does reduce the incidence of recurrence.

If it is true (particularly in the female) that certain tissue cells of the genitourinary tract are capable of taking viable gonococci within them and protecting such organisms from the effects of penicillin, then viable gonococci are released within the host when these cells are shed. Such viable gonococci could be released some weeks after the initiation of therapy, so that it is obvious that the presence of long-acting penicillin in such a patient would be a deterrent to auto-infection. Although this hypothesis has not yet been confirmed by clinical research, such action is warranted as a preventive measure until more is known about the disease in this regard.

The previous concept that a dosage of 160,000 units of penicillin over a 45-hour period represented the use of an excessive amount of drug must be considered fallacious, and higher levels of penicillin should be used over a much longer time than has been done previously. In this

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For acute attacks: Single dose of 75 cc. for adults; 0.5 cc. per lb. of body weight for children.

For 24 hour control: For adults 45 cc. doses before breakfast, at 3 P.M., and before retiring; after two days, 30 cc. doses. Children, 1st 6 doses 0.3 cc.—then 0.2 cc. (per lb. of body weight) as above.

1. Schluger, J. et al.: Am. J. Med. Sci. 233:296, 1957.
2. Bradwell, E. K.: Acta med. scand. 146:123, 1953.
3. Truitt, E. B. et al.: J. Pharm. Exp. Ther. 100:309, 1950.

REFER TO PDR
PAGE 612

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way the tendency of the gonococcus to develop further resistance to penicillin can be blocked.

Uncomplicated gonorrhea in the male is less difficult to diagnose and treat. In non-gonorrheal urethritis (NGU), it would be wise to take smears routinely on male patients to aid in distinguishing between gonorrhea and NGU. It must also be remembered that when occasional treatment failures of gonorrhea occur and NGU has been excluded cultures should be obtained and the susceptibility of the gonococcus to penicillin determined as a guide in therapy.

Before the advent of penicillin, diagnosis of syphilis was easy but treatment difficult. Following the availability of penicillin treatment has become simplified and diagnosis more difficult, this because of the rapid decline in incidence, the availability of a multitude of new serodiagnostic procedures and, a presumed increase in the incidence of diseases associated with biologic false-positive reactions.

Although reagin or Wassermann tests are no longer considered specific for syphilis, the newer tests (such as the Treponema Pallidum Immobilization test) are so considered. No serologic tests diagnose syphilis, their results merely informing of the immunologic status of the patient in relation to reagin and treponemal antibodies. Practically all the related treponemal diseases in man react to these test procedures, and certain antigenic components isolated from non-pathogenic treponemes will react with syphilitic antibodies.

While it is true that both false-positive and false-negative test results have been observed for all the treponemal tests, they occur in so small a number of cases when compared with reagin results that one of the special usefulnesses of the treponemal tests is in distinguishing the chronic biologic false-positive reactor from the patient with syphilis.

The RPCF test is the least expensive, most readily available as is the TPCF 60 test. Commercial antigen is available for both procedures, and the tests may be done in any competent laboratory. The Treponema Pallidum Immobilization (TPI) test remains available to all physicians and clinics through the resources of the State Health Department and the U.S.P.H.S.

While the new procedures in the serodiagnosis of syphilis are helpful, they are no substitute for the physician's knowledge. To best serve his patients, the physician must be well informed about syphilis as a disease, his patient, and the implication of the report he receives.◀

California Med., 91:179-184,1959.

Tetanus: Prophylaxis and Treatment

DONALD E. ROSS, M.D., and J. J. KRAUT, M.D.,
Los Angeles, California

▶*This condition is a possibility in every wound and will submit only to antitoxin among patients who have not been immunized. Prophylaxis is the best defense against tetanus, and careful debridement and irrigation the best treatment where the bacillus is suspected. Sensitivity tests should be made on allergy patients.*◀

Severe crushing injuries and compound fractures are threats to life *via* tetanus, particularly if contaminated with dirt, grass and other debris. Penetrating wounds, especially wounds made by splinters (but even minor injuries such as blisters or pricks from rose thorns or needles) are also frequent causes. Any burned surface is dangerous, for the bacillus of tetanus may be harbored under the blisters or encrustation.

Treatment

Early and thorough treatment of the wound is essential. No amount of antitoxin will prevent tetanus if dead tissue and foreign substances are permitted to remain deep in the tissues. Wounds should be washed thoroughly with soap and water and copiously irrigated with saline solution. Penetrating wounds should be uncapped by removal of the superficial skin. Some wounds may be excised. All should be opened wide to facilitate removal of all dead tissues, blood clots and foreign bodies. If bone, tendons, vessels or nerves are exposed, they must be covered by sliding the skin over the wound or by skin grafting. Debridement and cleansing in these cases must be meticulous.

The ideal prophylaxis against tetanus is active immunity, giving three tetanus toxoid injections of 0.5 cc. each, the second injection 30 days after the first, the third six months after the second. It is necessary to give a booster injection every four to five years. Following these subsequent doses, the blood antitoxin rises to a higher level than that produced by the first two or three doses. To be effective, the

course of toxoid inoculations must have been completed at least 30 days before the infliction of the wound. Toxoid given at the time of injury to a patient who has not had a toxoid series of inoculations is without value. In no such circumstances can toxoid be a substitute for antitoxin. Active immunization is particularly important for persons sensitive to horse dander because giving antitoxin to such a person, should the need occur, might be dangerous.

Diphtheria-Pertussis-Tetanus vaccine (DPT) is recommended for the first five years of life, the bivalent Diphtheria-Tetanus (regular) vaccine for ages six to 11 years, and finally the Diphtheria-Tetanus (adult) vaccine for persons 12 years of age and over, with a booster injection every five years. Parents and children old enough to remember should be made aware that injections of toxoid are being given, and should be firmly instructed that booster doses are necessary and impressed with the importance of being able to inform another physician should occasion arise that immunization has been carried out and the date of the last booster.

Required Precautions

Recently more than one-third of all deaths from tetanus in the United States in one year occurred in patients less than one year of age. Immunization of the prospective mothers by toxoid would give a measure of protection to the newborn infant.

Since there is risk in the administration of tetanus antitoxin, it is important to determine in which wounds use of antitoxin is advisable. In the more serious cases antitoxin is almost mandatory, assuming that there has been no active immunization. It may be decided to withhold antitoxin in the case of a superficial wound that can be excised or adequately cleansed. If antitoxin is necessary the physician should fully acquaint the patient with all the difficulties and risks.

The usual dose is 3,000 to 5,000 units although in cases of a very severe, mutilating injury, give 10,000 units or more. Sensitization increases with each subsequent dose and tetanus would be more difficult to treat if it should develop. Several days after its occurrence, a wound may not be too late for antitoxin, but 10,000 units at least should be given.

Inquire carefully as to allergic sensitivity, especially asthma precipitated by contact with horse dander before giving any antitoxin. Inject exactly 0.02 cc. of 1:10 dilution of antitoxin intradermally, the same amount of normal saline solution into the

other arm as a control. Observe for 15 to 20 minutes and if no local or constitutional reaction occurs, the required amount of antitoxin may be given subcutaneously with little fear of serious reaction. A positive reaction demands a desensitization procedure.

If the skin test for sensitivity to antitoxin is negative but there is history of allergic disease, the ophthalmic test may be advisable, response to which affords warning that any desensitization process or the administration of antitoxin may be hazardous. Performance of this test involves placing one minim of diluted horse serum (1:10 or 1:100) in the lower conjunctival sac of one eye, and one minim of normal saline solution in the other. Lacrimation, redness and itching following the instillation of the horse serum, appearing immediately or 15 or 20 minutes later, are positive results. The test is not without risk. Severe reaction may cause corneal injury and impairment of vision. To prevent this give one drop epinephrine 1:1000 intramuscularly immediately upon the appearance of the first sign of severe reaction.◀

California Med., 90:322-327,1959.

Prognosis for the Cancer Patient

Diagnosis and therapy requires an intimate knowledge of cancer and its effects on the host. Depending on its location, the lesion may press on a vital area in the brain or erode into a hollow viscus. Functioning tumors of the anterior pituitary gland in children produce gigantism, and acromegaly in the adult. A malignant tumor will produce severe malnutrition, particularly if ulcerated and secondarily infected.

The natural history of the cancer must be known. The mean survival time for patients with untreated cancer of the breast is 38 months, for those with untreated cancer of the esophagus 12 months. The smaller the cancer at time of detection the more likely it is to be circumscribed. Cancer of the uterine cervix of less than 1 cm. seldom spreads to the lymph nodes. The five-year survival rate for those with cancer of the breast less than 2 cm. is 74%, while that for those with cancer greater than 5 cm. is only 33%. In cancer of the breast 5-year survival rate is 65% when only the lowest level of lymph nodes is involved. When the highest level lymph nodes are involved the 5-year survival rate is only 28%. Melanomas, gliomas, and certain bone tumors have a very rapid downhill course. Others, such as the basal-cell carcinoma are of low grade malignancy. Patients with a keratinizing cancer of the uterine cervix have a 55%, those with the large-cell non-keratinizing type an 80%, and those with small-cell malignant tumor only a 20% 5-year survival rate. Unsuspected cancer of the cervix detected through the use of cytology usually is of the large-cell non-keratinizing type having a very favorable outlook.

A good local host reaction after irradiation usually means a better outlook for the patient. The presence of SR cells in the vaginal pool is frequently considered to convey a good reaction, as is the finding of larger normal cells of the cervix after irradiation.

Mast cells are reduced in numbers in benign tumors and are scarce in malignant tumors. They are observed in large numbers at the periphery of a malignant tumor, however, suggesting a defense mechanism.

Reagan, J. W., *Illinois M.J.*, 116:212,1959.

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"To those patients who had multiple metastases and metastatic lesions, Tigan was truly a godsend, enabling them to continue treatments and obtain relief . . . not obtainable in any other non-surgical way."[1] Successful in some of the most challenging conditions, such as radiation[1,2] or nitrogen mustard therapy,[3-5] Tigan is equally effective in all other situations calling for the prevention or control of nausea and vomiting. Travel sickness, pregnancy and gastrointestinal disorders are among the leading indications for Tigan. Three convenient forms: Tigan Capsules—100 mg, blue and white • Tigan Ampuls—2 cc (100 mg/cc) • Tigan Suppositories—200 mg.

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References: **1. J. A.** Lucinian and R. H. Boun, paper read at Colloquium on The Pharmacological and Clinical Aspects of Tigan, New York City, May 15, 1959. 2. H. E. Davis, Discussant, *ibid.* 3. W. B. Abrams, I. Roseff, J. Kaufman, L. M. Goldman and A. Bernstein, *New York J. Med., 59*:4217, 1959. 4. I. Roseff, W. B. Abrams, J. Kaufman, L. Goldman and A. Bernstein, *J. Newark Beth Israel Hosp., 9*:189, 1958. 5. B. I. Shnider and G. L. Gold, paper read at Colloquium on The Pharmacological and Clinical Aspects of Tigan, New York City, May 15, 1959. 6. M. W. Goldberg, *ibid.* 7. O. C. Brandman, *ibid.* 8. D. W. Molander, *ibid.* 9. W. S. Derrick, *ibid.* 10. B. Wolfson and F. F. Foldes, *ibid.* 11. W. K. Gauthier, Discussant, *ibid.* 12. L. McLaughlin, *ibid.* 13. W. Schallek, G. A. Heise, E. F. Keith and R. E. Bagdon, *J. Pharmacol. & Exper. Therap., 126*:270, 1959. 14. Reports on file, Roche Laboratories. 15. Personal communications.

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Idiopathic Hypertrophic Osteoarthropathy

A boy of 17 entered the hospital because of enlargement of the hands and feet. He had been well until two years before when painless swelling and enlargement of his hands and feet began, followed by involvement of the wrists, forearms, ankles and lower legs. Symptoms had been static for several months prior to admission. Diagnosis of acromegaly was made.

Swelling of the face, trunk and extremities 2½ years previously had been diagnosed as acute diffuse glomerulonephritis and treated by one month of bed rest. These symptoms had been preceded by a sore throat not accompanied by cardiac disease, painful joints or skin rash. The general health had been good. No relative was known to have limb enlargement or clubbing.

Except for obvious hypertrophy of parts, examination was uninformative. The patient was discharged without being given medication, and during a subsequent interval of five months the status of his extremities was unchanged and he remained asymptomatic.

About 50 cases of idiopathic hypertrophic osteoarthropathy are included in the world literature. This condition has its onset in males at or about puberty. Enlargement of parts continues for three or four years, slows and becomes static. Although not altering life expectancy, the condition often causes cumbersome disfigurement.

Baldwin, J. N., *New England J. Med.*, 261:592-595,1959.

Dexamethasone for Arthritis

A series of 19 patients with acute rheumatism, chronic rheumatoid arthritis, subacute polyarthritis, spondylitis anykylopoietica, erythema exudativum multiforme, lupus erythematosus, and bronchial asthma were treated with dexamethasone and the results compared with those obtained with prednisone therapy. Excellent results were obtained in six patients with chronic rheumatoid arthritis, acute rheumatism, and subacute polyarthritis and satisfactory results in another six with rheumatoid arthritis. The sedimentation rate was markedly reduced with dexamethasone in 16 patients, potassium levels in these patients being lowered or returning to normal. A slight increase in blood sugar level was observed in one. Glucose tolerance tests during dexamethasone treatment revealed an abnormally low tolerance in two patients and a normal curve in five. Dexamethasone was shown to be six to eight times as effective as prednisone.

Foreign Letters, *J.A.M.A.*, 171:236,1959.

Relation of Septic Arthritis to Intra-articular Injections of Hydrocortisone Acetate

Intra-articular injection of corticosteroids is related to septic arthritis in two principal ways:

1. Infection may be directly introduced into the synovial cavity by the procedure.

2. Injection may be made into an already septic joint because of a hasty and misguided attempt to relieve the patient's suffering without adequate preliminary study.

These errors may be avoided by due consideration of differential diagnosis, appropriate studies of synovial fluid, x-ray examination, and rigid surgical aseptic techniques. There is also suggestive evidence that corticosteroid injections into inflamed joints may lead to localization of circulating organisms from remore foci of infection (probably through inhibition of local defense mechanisms), thereby leading to septic arthritis.

Intra-articular injections of hydrocortisone acetate and its analogues have proved practical adjuncts in the treatment of painful diseases of joints and bursas. The procedure is not innocuous and must be used with care and due regard paid to its deleterious effects. It has also been demonstrated that septic arthritis is related to corticosteroid injection through direct introduction of contaminated material into the synovial cavity, failure to recognize existing septic arthritis before injection and probably by interference with local defenses against bacteria. This complication is serious, resulting in prolonged discomfort, disability and occasionally death.

Gowans, J. D. C., & Granieri, P. A., *New England J. Med.*, 261:502-503,1959.

"Tight Filum Terminale" Syndrome

Although this loosely designates a number of clinical entities, the syndrome represents a recognizable clinical picture. Progressive spastic paralysis of the lower extremities with or without urinary difficulties in the adolescent patient should suggest this possibility. Spina bifida occulta or dimpling of the skin in the lumbosacral or sacrococcygeal area is sometimes seen. There may be skeletal dysraphia or even diastematomyelia. Progressive spastic paralysis while patients are under observation for other conditions should arouse suspicion of the syndrome.

In one case, a woman of 33 on one or two occasions noted loss of a few drops of urine while she was up and about. She was asymptomatic until two years later, when she consulted her physician because of recurrent pains in the right lower abdo

men. Appendectomy was performed, and cysts in both ovaries punctured. Beginning four years later and continuing for three years, bouts of urinary incontinence, urgency and dribbling required a perineal pad. Alterations of bowel habits caused her to use laxatives and enemas. Relaxation of the anal sphincter beginning one year later caused soiling of undergarments by feces One year later, she had pain in the lower back, the right popliteal region and foot. Weakness and heaviness of the right leg and foot ensued. All symptoms gradually progressed. Coughing, sneezing, and straining, lifting, jarring, or riding in a car, aggravated the pain in the back and in the right leg. Residual urine at this time was 200 and 300 cc. A myelogram (pantopaque) was reported to be normal, as was CBS fluid. A year later, 1400 cc. of residual urine was found with overflow incontinence. Another myelogram disclosed nothing abnormal.

When seen following year, positive findings were bilateral Babinski reflexes, weakness of the lower extremities (greater on the right), sensory loss in sacral rootlets with reduced sensitivity to touch, pain and temperature. Probable diagnosis was an intramedullary tumor or some rare type of sacral syringomyelia. Myelogram disclosed nothing. Total proteins in the cerebrospinal fluid was 10 mg. per 100 cc. A roentgenogram of the lumbar spinal column revealed nothing. No congenital defect of the skeletal system was found. There was a small dimple near the first sacral vertebra.

Under general anesthesia minimal bilateral laminectomy was carried out and the dura opened. The conus medullaris was not located at this level. Exploration between the third and fourth lumbar vertebrae revealed no cauda equina. The conus, found attached to the dura at the level of the first sacral vertebra, had undergone degenerative changes. Anteriorally there was a tense fibrous band resembling the usual filum terminale.

The continued traction exerted by a tight filum terminale will produce degenerative changes in the lower part of the spinal cord. In such instances, early surgical intervention might prevent irreparable, progressive neurologic changes by determining the presence or absence of an abnormally low-lying conus medullaris of the spinal cord, a tight filum terminale, or both. Roentgenograms of the thoracic and lumbar vertebrae, as well as contrast myelography, should be included.

Uihlein, A., *Minnesota Med.*, 42:394-398,1959.

Current Concepts of Rheumatoid Arthritis

Despite intensive investigation in the past decade the cause of rheumatoid arthritis remains unknown, and the treatment is still primarily symptomatic. A basic conservative program has been used extensively and is often sufficient alone or with the addition of one of the antirheumatic drugs.

The disease occurs most frequently in persons 30 to 45, but no age is spared. Synovitis is usually the first manifestation. There are many non-articular cases. The classical form occurs more in females than in males, the ratio being 3 to 1. The onset may be insidious or rapid. Remissions can occur spontaneously and without residual damage.

A mild anemia and an elevated ESR are common when the disease is active. By various techniques serological tests can be positive in 70 to 90% of cases. If subcutaneous nodules are present, the test can be positive in almost 100%.

Relief of pain is the primary consideration in treatment. Twenty-four hours of rest for the severe, acute illness and lesser periods if the condition is more moderate is recommended until the acute phase has subsided or the rate of improvement has become static. Heat and specific exercises are started as soon as possible. Aspirin in generous amounts will give comfort. At times, a stronger analgesic such as codeine may be needed. About 40% of patients so treated will recover sufficiently to obtain remission and return to work. The use of corticosteroids in the treatment of rheumatoid arthritis has proved their value. Although they rarely induce a true remission, they enable the patient to lead an active and useful life. They should not be used routinely. Small doses are required with the newer drugs of this class. The untoward reactions remain the same, but occur less frequently. The real contraindications to steroid therapy are peptic ulcer, osteoporosis, diabetes, tuberculosis and other active infections, also psychoses and senile psychoneuroses. If single joint flares or continue to give trouble, intra-articular injections of hydrocortisone, prednisolone, or prednisolone suspensions are advisable, rather than increased systemic dosage.

Deformities may ultimately require orthopedic care. Antimalarials have given gratifying response in a large percentage of patients, untoward effects with these drugs not being serious and disappearing upon discontinuance.

Minno, A. M., *Pennsylvania M.J.*, 62:1670,1959.

Anticoagulant with Digitalis Therapy for Combined Valve Disease and Enlarged Heart

Treatment of patients with combined valve disease and enlarged heart presents a difficult problem since treatment of the congestion predisposes to the danger of embolism, this the result of increasing the contractile strength of cardiac muscle by intensive digitalization. Often, no effect can be obtained by other means such as bed rest, restriction of salt or use of diuretics. For such cases a new therapeutic regimen consists in giving digitalis along with protective anticoagulant therapy. Treatment is usually started with dehydration and maintenance of strict bed rest. If the desired effect is not reached with these measures, anticoagulant therapy is instituted. Two to three days later a purified digitalis preparation is cautiously started. Anticoagulant therapy is continued for the usual prolonged period of time.

Although this combined therapy may not abolish the possibility of embolism, it lessens its risks. In a small series neither embolism nor any side effects occurred with this treatment. Value of this therapy can be assessed only from experience in a large number of cases.

Jonkias, J., *Brit. M.J.*, 2:365,1959.

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Pneumonectomy for Tuberculosis

During a period of 13 years, the proportion of pneumonectomies in 1496 resections done in tubercular patients decreased to 1.4%, that of lobectomies to 94.4%. The number of segmental resections increased to 84.2%. Of the patients admitted five years after those hospitalized initially, more than 55% had cavities when first seen. More than 70% of the patients discharged recovered with bed rest and medical treatment alone. Resection is now considered indicated if the foci remain unchanged after seven to 10 months of strict bed rest and treatment, if the sputum is positive, and if resistance of the tubercle bacilli is manifest or imminent.

Evaluation of a series of 1316 patients undergoing surgery revealed a primary death rate after pneumonectomy of 8%, after segmental resection of 0.25%, and after combined lobectomy and segmental resection of 0.6%. The late mortality rate was 2%. Bronchopleural fistula and empyema were the most frequent causes of death. Bronchial fistulas occurred in 4%, appearing during the first half-year. Relapses occurred in 74 (5.7%). The sputum became negative in 97.6%, and 89.6% regained full ability to work. Of 637 patients whose progress was followed for more than five years, 98.1% had negative sputum and 93.8% were fully able to work. Thoracoplasty was resorted to for pretreatment in isolated cases.

Intrapleural and extrapleural pneumothorax are rarely indicated and phrenic nerve operations have become obsolete. Effective follow-up treatment currently includes administration of para-aminosalicylic acid (PAS), streptomycin, and isoniazid (INH), either together or in combination of any two. To prevent development of resistance, the proper time for removal of the main focus must be selected.

Foreign Letters, *J.A.M.A.*, 171:236,1959.

Skeletal Metastasis From Carcinoma of the Colon and Rectum

Tumors of the breast, prostate, bronchus, thyroid and kidney are prone to bone metastasis. Skeletal metastasis from carcinoma of the colon and rectum occurs often enough to be of serious concern. Although metastatic carcinoma is by far the most common malig-

nant bone tumor, x-ray skeletal survey might reveal many additional carcinoma foci. X-ray alone has limitations, evidenced by a study in which 50% of examined vertebrae pathologically shown to harbor malignant implants did not show evidence disease diagnosable by x-ray studies.

In autopsy series skeletal metastasis has been from 15 to 30% of all patients dying of carcinoma, depending on the thoroughness with which the bones are examined grossly and microscopically. In a large series of cancer patients, 27% of the entire group showed skeletal metastasis. More than 2/3 of breast, 1/3 of lung, and 1/4 of renal carcinoma observed in this 27% had spread to one or more bones. Carcinoma of the pancreas in 13%; of the rectum in 13%; stomach in 11%; colon in 9%; and ovary in 9% also spread to the skeleton. Almost any malignant tumor of almost any organ may metastasize to any bone and result in a rather common or a most bizarre clinical and x-ray pattern. The nearer a bone is to the site of primary cancer the greater the chance of a metastatic deposit.

Metastasis of carcinoma of the gastrointestinal tract to bone is said to rarely occur because the portal system filters out the cells. Consideration has been given to spread, especially to the skull, pelvis and spinal column via the paravertebral veins. This metho of spread would seem importa when visceral organs and lung have escaped metastatic spre but osseous spread is evide Evidence of the importance of t venous route of spread from t colon continues to accumulat The higher the grade of mali nancy the more frequent is ve involvement.

From carcinoma of the col and rectum, the vertebrae a the favorite sites of skeletal m astasis—as a rule, multiple. average of two years had elaps following the original diagno before skeletal metastasis beca evident in many case repor Both osteoclastic and osteoblas types of metastasis (mostly t former) have been reported. notable feature of many of the lesions is a proliferative reacti of expanded periosteum. Pain frequently severe, patholo fracture not uncommon. With exception of hypernephroma the prostate, the site of the p mary tumor often cannot be ide tified by the microscopic appe ance of the metastatic lesions bone.

Deep x-irradiation may be p liative. The dosage should not pushed to the point of induci radiation necrosis nor of enha ing the likelihood of patholo fracture.

Wooldridge, B. F., *Missouri Med.*, 56:1363-1365,1959.

Chlorpropamide in Diabetes

Chlorpropamide is a new hypoglycemic sulfonylurea compound structurally related to tolbutamide. A total of 118 adult diabetics selected as being most likely to benefit form this therapy have been treated. More than half these cases have been receiving the drug for 6 to 14 months. All were ambulatory unless hospitalized for some other reasons.

The optimum diet for each patient was determined and continued. All patients recorded urine sugar and acetone tests four times daily for the first two weeks. Blood sugar (postprandial) tests were made once weekly, oftener if indicated. Blood counts, blood urea nitrogen and thymol turbidity tests were done at the same time. Newly discovered cases without previous therapy were tried on diet alone for a week or two. To previously insulin-treated patients, chlorpropamide was given alone, 250 mg. once or twice daily. For most patients on tolbutamide, only one dose of 250 mg. or less of chlorpropamide was adequate. Therapy was considered unsuccessful if hyperglycemia was uncontrolled after seven to 10 days' treatment, or if ketosis developed.

Of the 118, 79% were successfully controlled. Chlorpropamide was successful in smaller dosage in a number of cases either poorly controlled or having been secondary failure on tolbutamide. Chlorpropamide should be used only in the treatment of stable non-ketotic adult diabetics, whose condition developed after age 40. Dietary control is essential for the treatment of all diabetics, chlorpropamide not being required when diet alone is adequate.

Pennock, L. L., *Pennsylvania M.J.*, 62:1537-1539,1959.

Acute Massive Digitalis Poisoning Treated by a Chelating Agent

The heightened sensitivity of the diseased myocardium to digitalis, as manifested by toxic responses to average or small doses, is well established. Chelating compounds acting by removing calcium from the ionic milieu have been useful in the treatment of digitalis intoxication in patients with heart disease.

In a cited case a single woman of 49 was admitted one day after

having swallowed 100 tablets of digoxin 0.25 mg. She had been found to have atrial fibrillation. Although the aphasia had cleared rapidly, there had been some residual left-sided paresis. The atrial fibrillation had been paroxysmal and functional, brought on by coffee, tobacco and emotional upsets. Six months prior to admission the patient had discontinued taking digitalis and quinidine because of the virtual cessation of paroxysms. Three hours after taking the large quantity of digoxin, violent vomiting ensued and persisted until the following day, when the patient was admitted in an obviously dehydrated state.

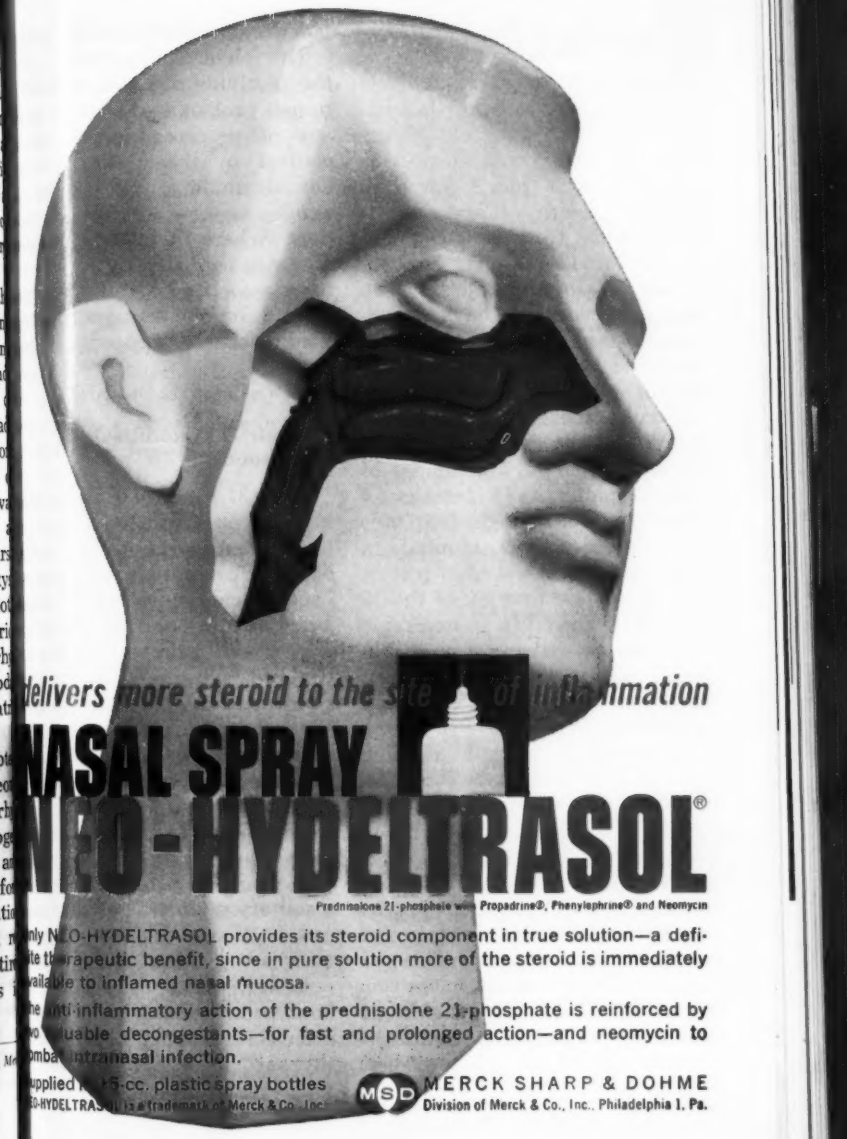
On admission her temperature was 100.8°, pulse 40 and irregular, respiration 24, and blood pressure 140/50. The cervical veins were not distended and there was no cardiac enlargement. Ventricular rate was slow and irregular. A faint systolic murmur was best heard at the apex and left parasternal border. Neurologic findings were consistent with a left hemiparesis. Blood urea nitrogen was 34 mg./100 ml. The first ECG revealed long periods of sinus standstill with irregular nodal escape and premature beats, digitalis effect, and first degree atrioventricular block.

Rapid intravenous infusion of 40 mEq. of KCl and 500 ml. of 5% glucose did not alter th ECG. Disodium versenate (ED TA) therapy, 375 mg. in 250 m of glucose and water, was the started. Tracing soon showed Wenckebach - phenomenon var ant. In 20 minutes there was normal atrioventricular conduc tion and only a rare prematur nodal beat.

A period of 40 minutes with out therapy then ensued, tracin during that time demonstratin the recurrence of sinus stand still. An additional 400 mg. disodium versenate was then a ministered in 250 ml. of solutio after which a brief period normal impulse formation w again established. Tracings intervals after this second cours showed atrial flutter, paroxy mal atrial tachycardia (bo with varying degrees of atri ventricular block), nodal rh thm, sinus standstill with nod escape beats and premature at al beats.

Five days after the attempt suicide there was spontaneo reversion to a regular sinus rh thm. The blood urea nitrog fell to normal with fluid a electrolyte replacement. Befo transfer to another institutio for psychiatric and physical r habilitation the ECG was entir ly devoid of abnormalities contour or rhythm.

Bernstein, M. S., et al., *New England J. M* 261:961-963,1959.



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Management of Recurrent Aphthous Stomatitis

Thirteen consecutive subjects with the major form of this disease, in whom aphthous ulcers were present continuously or with not more than a few days freedom, were placed on a double-blind treatment trial continued for 12 months. The patients remained on each of two preparations for 28 days. Treatment was instituted with hydrocortisone hemisuccinate linguets 2.5 mg., given six times daily for 28 days, then quinalbarbitone sodium 50 mg. given twice daily for another 28 days. Mean age of the 13 patients (9 females, 4 males) was 39 (range, 28 to 60). The disorder was familial in three instances.

It is notable that six of the 13 patients showed a remarkable response to the initial consultation before any therapy had been instituted, while three remained totally free from lesions during the follow-up period of nine months. An additional three relapsed after a month or two, then proved resistant to all therapy including hydrocortisone. Placebo lozenges produced a reduction of over 50% in the frequency and duration of ulcer in six of the 13 patients, while local application of prednisolone or hydrocortisone was capable of inducing a sustained remission where all other measures had failed in about 25% of the case

The physician, sedation, an the resolving of social and emo tional problems do more tha any other procedures to effec control in those cases when chronic anxiety, or depression exogenous origin is clearly ev dent. Where no such exogeno stress or endogenous abnorma ity is associated with the disea steroid therapy remains the mo useful of the procedures em ployed.

Sircus, W., *Brit. M.J.*, 2:804-806,1959.

Chronic Thyroiditis in Childhood

Only 31 cases of this disord have been reported, most them after operation for a goit causing pressure symptoms because carcinoma could not ruled out in a nodular goiter. only a few instances was the n ture of the disease suspected a confirmed by needle biop With the newer diagnostic te niques, nonoperative diagno may be made if thyroiditis once considered.

Thyroiditis usually causes largement of the entire gla while early carcinoma is usua a solitary nodule or enlargem of a portion of the gland. Sym toms are a sense of fulness pressure, mild dysphagia a hoarseness. Most patients euthyroid or only mildly hyp thyroid. Surgical procedu

hasten the onset of hypothyroidism.

There is no specific laboratory test, but routine tests of thyroid function may be suggestive. The I^{131} uptake alone is not helpful, failure to increase it after administration of thyrotropin being suggestive of thyroiditis. If the gland is diffusely enlarged, needle biopsy may be helpful. Nearly all solitary nodules should be excised for study. If there is still doubt after all studies have been performed, surgical biopsy should be done to establish the diagnosis.

Therapy is thyroid extract, whether the patient is hypothyroid or euthyroid. This will suppress thyrotropin activity if used in dosages of 60 to 240 mg. daily, and in most cases will cause a reduction in size of the goiter within three to six months. If there is a wide difference in protein-bound iodine and butanol-extractable iodine values, this will also be corrected with thyroid therapy. Thyroid extract should probably be continued indefinitely to reduce the size and prevent recurrence and to prevent hypothyroidism in the adolescent. If thyroid therapy is ineffective, surgery may be necessary later for cosmetic reasons or to relieve obstructive symptoms.

Brown, H., & McGarity, W. C., *J.A.M.A.*, 171:1182-1186,1959.

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Doctors and the Law

CHARLES J. FRANKEL, M.D., L.L.B., *Editor*

Will the National Labor Relations Board assert jurisdiction over a labor dispute between a proprietary hospital and its employees?

This question was passed on by the National Labor Relations Board in *Matter of Flatbush General Hospital* and *Local 144, Hotel and Allied Service Employees Union, Building Service Employees International Union, AFL-CIO,* 126 NLRB No. 7 (1960). After the union began picketing for recognition as exclusive bargaining agent of its employees, the hospital filed a petition requesting an immediate election to determine whether the union represented a majority of its employees.

The union moved to dismiss the petition on the ground that the hospital, a proprietary one, is not engaged in commerce and that, even if statutory jurisdiction is found to exist, the impact on commerce of the hospital's operations is not sufficient to warrant assertion of jurisdiction. For the first three months of its operations, the hospital's gross revenues were approximately $140,000 and its purchases of supplies, medicines and materials for operations were valued at about $58,000, of which about $34,000 worth came directly or indirectly from out-of-State. It was estimated that the hospital's annual gross volume of business, at projected full capacity operation, would be $1,000,000. Most of the hospital's patients are local residents.

The Board said that, in the past, it had asserted jurisdiction over proprietary hospitals only where the hospital was located in the District of Columbia, where the hospital's operations vitally affected national defense or where the hospital was an integral part of an establishment whose operations met the Board's jurisdictional standards. The Board said that, although the hospital has sufficient inflow of goods from out-of-State to meet the requirements for a finding of legal jurisdiction, the

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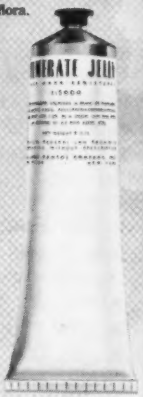
Prescribe: "Nylmerate Jelly with applicator"—5 oz. tube, also available in refill tube only. Simplé to use . . . Applicator-full intravaginally morning and night preceded by a Nylmerate Solution water douche. Include treatment through menstrual period.

Available only on your prescription.



ACTIVE INGREDIENTS

Polyoxyethylenoxyethanol	0.10%
Phenylmercuric Acetate	0.02%
Boric Acid	1.0%

In a gum base with pH adjusted to 4

NYLMERATE SOLUTION CONCENTRATE

a therapeutic vaginal douche of choice

Excellent adjunct in the management of monilia and trichomonas vaginal infections. Restores normal vaginal flora through a 3-prong attack. Low surface tension aids in reaching the innermost recesses where organisms flourish. Unlike vinegar, affords a controlled pH of 4.1 in dilution and is effective in any vaginal pH. Broad range activity against protozoa—bacteria—and fungi. Well suited for office use in swabbing vaginal vault.

Available only on your prescription (eliminates excessive and unwarranted douching). Specify—Nylmerate Solution Concentrate pint bottle with measuring cap. Prescribe two tablespoonfuls or one capful to two quarts of water twice daily. As a prophylactic use once a day through two menses.

ACTIVE INGREDIENTS

Phenylmercuric Acetate 0.2% in a buffered solvent of Alcohol 50%, Acetone 10% and de-ionized water q.s., added certified color with pH adjusted to 4.9.

Literature available

HOLLAND-RANTOS CO., INC.
145 HUDSON STREET · NEW YORK 13, N.Y.

operations of this class of proprietary hospitals, although not wholly unrelated to commerce, are essentially local in nature and the effect on commerce of labor disputes involving such hospitals is not sufficient to warrant the exercise of the Board's jurisdiction. The conclusion that such hospitals are local in character rests primarily on the facts that they serve local residents and their operations are subject to close regulation by the states.

The hospital contended the Board's refusal to assert jurisdiction will leave hospitals of its type in a legal "no-man's land," especially since the state labor board has held that it has no jurisdiction over labor disputes involving proprietary hospitals. The Board said the labor relations of proprietary hospitals will not be left in "no-man's land" because the new labor law allows States to assume jurisdiction where the Board does not assert its legal jurisdiction. Because of the public health and safety involved in their operations, proprietary hospitals and their personnel are subject to State regulation in a number of particulars and it is therefore likely, said the Board, that, if labor disputes arise involving such hospitals, the States will act to regulate the disputes.

▶*Can a doctor refuse to testify, in a pre-trial deposition hearing, as to matters communicated to him by patient when patient himself, for purpose of preserving by record his testimony, has given a pre-trial deposition covering the same matters?*◀

The Court of Appeals of Cuyahoga County, Ohio, passed on this question in 1956 (*In re Loewenthal's Petition,* 134 N.E. (2d) 158. The patient was treated by the doctor for injuries suffered in an automobile accident. The patient brought a personal injury action against the person allegedly responsible for the accident and, for the purpose of perpetuating his testimony, gave a pre-trial deposition stating in detail the injuries allegedly incurred, what he told the doctor in regard thereto and what treatment the doctor administered. Thereafter, defendant in the personal injury action subpoenaed the doctor for purpose of questioning him, by way of deposition, as to his patient's injuries and the treatment thereof, solely for the purpose of perpetuating the doctor's testimony. The doctor refused to answer any questions on the ground he did not have the patient's consent to do so. Defendant in the personal injury action contended that the plaintiff in such action, by giving his deposition concerning the doctor - patient relationship, waived the privilege and the doc-

tor was therefore required to answer.

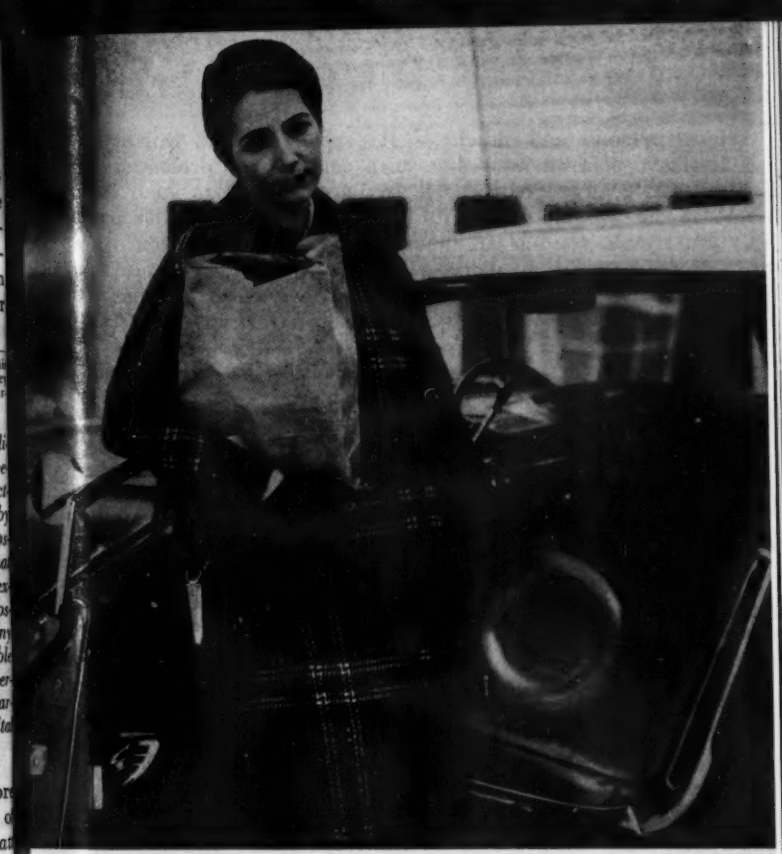
The Court said that the statute relating to privileged communications provides that a doctor may testify by express consent of the patient and if the patient voluntarily testifies, the doctor may be compelled to testify on the same subject. However, the patient here gave only a deposition for the purpose of perpetuating his testimony. The narrow issue is thus whether this constitutes such a waiver as to allow the defendant in the personal injury action to take the doctor's deposition. It is provided by statute that testimony may be taken by affidavit, by deposition or by oral examination. The statutes further provide that a deposition of a witness may be used only if he does not reside in or is absent from the county where the action is pending or is unable, because of death, age, infirmity or imprisonment to attend court. When the patient gave his deposition he was testifying as a witness even though the deposition might never be used in the case which was pending. The Court said the patient's deposition could not be offered in evidence if he was available to testify in person and that the same was true as to the doctor's deposition. However, the patient by giving his deposition as to his injuries and the doctor-patient relationship waived the privilege, but only insofar as deposition hearings are concerned. The doctor can be compelled to testify on deposition on the same subjects even though the occasion to use the depositions never arises.

Editor's Note: The doctor confronted with this type of situation should consult an attorney for advice rather than rely on a "do it yourself" attitude.

►*Can a public hospital deny a licensed doctor staff membership because of past conduct which subjected him to disciplinary action by board of medical examiners? Is hospital's rule valid, which provides that only doctors whose background, experience and training insures (in hospital board's judgment) that any patient will be given the best possible care, be admitted to staff membership? Is a doctor entitled to a hearing on application for public hospital staff membership?*◄

These questions were before the California District Court of Appeal, Third District, in *Wyatt* vs *Tahoe Forest Hospital District*, 345 P.(2d) 93 (1959). Plaintiff, a licensed doctor, applied for membership on staff of defendant, a public hospital. The hospital is the only one within a 35 mile radius. Hospital's board of directors rejected the application. Plaintiff then sought a hearing which was denied.

According to record considered by hospital's board, consisting of communications from var-



norectal comfort in minutes For full symptomatic ontrol in hemorrhoids, proctitis and pruritus ani *start* treatment with 2 nusol-HC suppositories daily for 3 to 6 days to eliminate all inflammatory mptoms rapidly and safely. Then *maintain* lasting comfort with 1 regular nusol suppository morning and evening and after each bowel movement. either product contains analgesics or narcotics, will not mask serious ctal pathology.

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AN-HS02

ious persons and much of it hearsay, plaintiff was first admitted to practice in 1930. In 1936, he was charged with unprofessional conduct in that he procured an illegal abortion. In 1939, his license was revoked on charges he had performed an illegal abortion. His license was reinstated in 1940 and he was placed on probation for five years. In 1941, plaintiff was reprimanded for violation of the terms of his probation. Also, in 1933, a complaint, charging plaintiff with unprofessional conduct in that he aided and abetted an unlicensed person to practice medicine, was dismissed and an admonition issued. In 1942, the board of medical examiners revoked plaintiff's license for violation of the terms of his probation on findings that he had procured illegal abortions on two persons and had been found guilty of the offense of maliciously and willfully disturbing the public peace. The board's decision was reversed by a court.

The statute under which defendant hospital was established empowers its board of directors to make rules and regulations for its administration and government. Such rules are to provide for the organization of doctors permitted to practice in the hospital into a staff and staff membership is to be limited to doctors "competent in their respective fields, worthy in character and in professional ethics" and subject to such limitations with respect to the practice of medicine as the board may find to be in the best interest of the public health and welfare. The hospital adopted a rule which states: "Membership to the medical staff shall be limited to those physicians and surgeons licensed to practice in the State of California, whose background, experience and training insures, in the judgment of the Board of Directors, that any patient admitted to or treated in the Tahoe Forest Hospital will be given the best possible care and professional skill." The rule further provides that possession of a license to practice in California is not to be determinative of an applicant's qualifications, competence, character or suitability.

Plaintiff contended that, being a licensed doctor, he is entitled to practice in a public hospital. The Court said a licensed doctor does not have a right *per se* to practice in a public hospital because the statute gives the boards of such hospitals the power to make rules limiting staff membership. However, such limitations must be reasonable. The Court said it did not believe that a doctor whose license was unrevoked and who is in good standing can be denied the right to practice in a public hospital

merely because of past conduct which subjected him to disciplinary action by the board of medical examiners; if he is to be excluded it must be for an existing cause. The record here, largely hearsay, showed plaintiff had been guilty of improper conduct in the past. The test to be applied by a public hospital's board is not an applicant's past wrongful conduct, but whether he is competent in his field, worthy in character and professional ethics at the time of application. The board of medical examiners has determined, after disciplinary action, that plaintiff should be permitted to practice. In the absence of any showing of improper conduct by plaintiff since he was disciplined, it would seem that his exclusion was arbitrary. It should also be noted, said the Court, that the hospital's rule for admission to staff membership is too vague and uncertain to be used as the basis for excluding an applicant. What is the best possible care and professional skill? Would it limit staff membership in the hospital to those who are recognized authorities in their respective fields? By what standards does the board, all lay persons, determine what is the best possible care and professional skill? A public hospital, in prescribing rules for those who wish to serve in the hospital, must establish rules which are clear, not vague and not ambiguous or uncertain. The rule adopted by defendant hospital's board of directors does not meet this test, because the standard set is such that admission to the staff can depend on the directors' whims and caprices, and it therefore may not be used to exclude plaintiff.

Plaintiff further contended he was entitled to a hearing on his application. The Court agreed, saying it was common knowledge that a doctor not permitted to practice his profession in a hospital is, as a practical matter, denied the right to fully practice his profession. The statute under which the hospital was established provides that staff membership is to be limited to doctors competent in their respective fields and worthy in character and professional ethics. Where a board is empowered to ascertain facts on which may depend the right to practice a profession, the board in exercising such power performs a quasi-judicial function. In making its decision the board must act fairly and its decision must be based on sufficient evidence. Plaintiff, therefore, has a right to a hearing to determine whether his qualifications meet the requirements established by law.

►*Is the value of food and lodging,*

Helps Revitalize Bone and Muscle Tissue

Improves Mental Competence

Analeptone-Anabolic offers a new approach to the treatment of aging patients by providing safe, well-tolerated, decisive medication, to counteract diminishing skeletal muscle powers, osteoporosis, and to help restore mental faculties.

Decisive in stimulating muscle and bone anabolism, and enhancing the patient's sense of well-being and vigor.
Decisive in counteracting cerebral anoxia, depression, confusion and mental debility.

FORMULA: Each tablet contains: pentylenetetrazol 50 mg., methyltestosterone 0.83 mg., ethinyl estradiol 0.0015 mg., strontium salicylate 450 mg.
DOSAGE: Usual dose is two tablets, three or four times daily.
SUPPLIED: Bottles of 100 tablets.
PRECAUTIONS: This preparation should not be used in patients who have established or suspected mammary, prostatic or other genital malignancy.

ALSO AVAILABLE:

ANALEPTONE® ELIXIR. Each teaspoonful (4 cc.) contains: pentylenetetrazol 200 mg., niacin 100 mg., peptenzyme elixir q.s. Supplied in bottles of 8 fl. oz.

ANALEPTONE® TABLETS. Each tablet contains: pentylenetetrazol 100 mg., niacin 50 mg., pepsin 1:10,000 5 mg.

SUPPLIED: Bottles of 100 tablets.

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R&C REED & CARNRICK / Kenilworth, New Jersey

furnished psychiatrist at state mental institution for convenience of the employer, taxable as compensation where Treasury Department revoked ruling, which had been in effect for many years, under which such items were not taxable as compensation, and issued new ruling declaring such items taxable as compensation?◀

The question was passed on by by the U. S. Court of Appeals, 2nd Circuit, in *Diamond* vs *Sturr*, 221 F.(2d) 264 (1955). Plaintiff, who for a number of years had been employed as a psychiatrist at mental institution operated by State of New York, was required as a condition of employment to reside on premises. Building in which plaintiff lived with his family also housed an assortment of mental patients, some noisy, some profane, some disturbed. The only play space plaintiff's daughters had was in an area traversed by hospital traffic, including ambulatory mental patients. When plaintiff began to work at the hospital, the Treasury Department's Regulation 111 provided that, "If . . . living quarters or meals are furnished to employees for the convenience of the employer, the value thereof need not be . . . added to compensation otherwise received." A Treasury Bulletin interpreting this regulation stated that, "As a general rule, the test of 'convenience of the employer' is satisfied if living quarters or meals are furnished to an employee who is required to accept such quarters and meals in order to perfom properly his duties." The Court said that under these circumstances—the meagerness of the facilities furnished, the requirement that plaintiff live at his post of duty and be available for call at all times, the absence of any showing that the food and lodging was regarded by the parties as compensation—the food and lodging furnished plaintiff was not compensation and not taxable, at least until the interpretation of the regulation was changed.

At the start of the taxable year in question, the Treasury Department revoked an earlier ruling, applicable to employees of mental institutions of the State of New York, and ruled that the value of food, lodging and maintenance furnished employees, whose salaries were classified under the New York Civil Service Law, as plaintiff's is, was compensation for federal tax purposes. The new ruling was without reference to whether the employee received significant economic benefit from the food and lodging and the factors of whether the employee was required to live on the post and be constantly available for duty were specifically disavowed as relevant in determining whether the maintenance

furnished was compensation. This is contrary to the "convenience of the employer" test. Regulation 111 and its previous interpretation had been in existence, in substantially the same form, since 1920. The Court said that Treasury regulations and interpretations long continued without substantial change, applying to unamended or substantially reenacted statutes, are deemed to have received congressional approval and have the effect of law. Since the "convenience of the employer" test as a measuring-rod of compensation has persisted through Treasury interpretations and the Tax Court throughout years of reenactment of the Internal Revenue Code, it constitutes the applicable standard for the tax year in question and, since the food and lodging furnished plaintiff were clearly for his employer's convenience, they are not taxable as compensation.◀

Cancer in Children

Cancer is second only to accidents as a cause of childhood mortality. Although this relative importance of cancer as a cause of death is due primarily to the lowering of the death rate from infectious diseases, some neoplasms (such as leukemia) have shown an actual increase in incidence. Over one-half of the cases occur among those less than 4 years, the lowest incidence being in the 5 to 15 age group.

Ninety per cent of childhood neoplasms are found in the blood-forming organs, connective tissue, and neural tissue, or are tumors of embryonal or mixed tissues. Those of nerve tissue and associated structures reach a peak before age five. The organs most frequently involved are the brain, paravertebral ganglions, kidney, lymph nodes and bone marrow, and soft somatic tissue. Neuroblastoma accounts for 20% of the total cases, half of these before age two, and three-fourths before age four. Leukemia is the commonest single malignant disease in young children, being responsible for 30 to 40% of all deaths in this category. Over the past 20 years there has been a steady and rather sharp increase in incidence of this disease, particularly in infants.

Tumors of the central nervous system constitute 5 to 10% of childhood malignant disease. A high percentage are congenital or of embryonic origin. Hereditary factors play an important familial role in the etiology of cancer in the 0 to 15 age group.

Cohen, L. S., & Thomison, J. B., *Am. Practit. & Dig. Treat.*, 10:1149,1959.

The Doctor Builds His Estate

Prepared monthly by the Research Department of Bache & Co., 36 Wall Street, New York 5.

These monthly articles point out one method by which the physician may overcome the handicap imposed upon him by taxes on the bulk of his income at normal rates, as opposed to the capital gains tax open to many business men. One solution is systematic investment of current income in securities.

Without attempting to forecast the market's actions over the coming months, we believe that electric utility common stocks should occupy an important role in almost any investment portfolio. From a defensive standpoint, price declines should be largely limited to those necessary to bring yields to a more normal level in relation to interest rates, while in a more positive vein it is possible that the outlook for continuous, though moderate, earnings growth could engender considerably higher prices.

Last year, electric utility common stock prices moved generally sideways, after recording a 31% advance in 1958. With an estimated gain in per share earnings of about 5%, the average price-earnings ratio declined from close to 19 times in March, 1959, to about 17 times at present, an earnings multiplier figure close to the 16 times figure which we believe can be considered a reasonable norm with a 5% earnings growth rate. Thus, while prices of electric utilities have not declined in general to a level where in our opinion, the group can be considered cheap, neither do these stocks on average appear vulnerably overpriced.

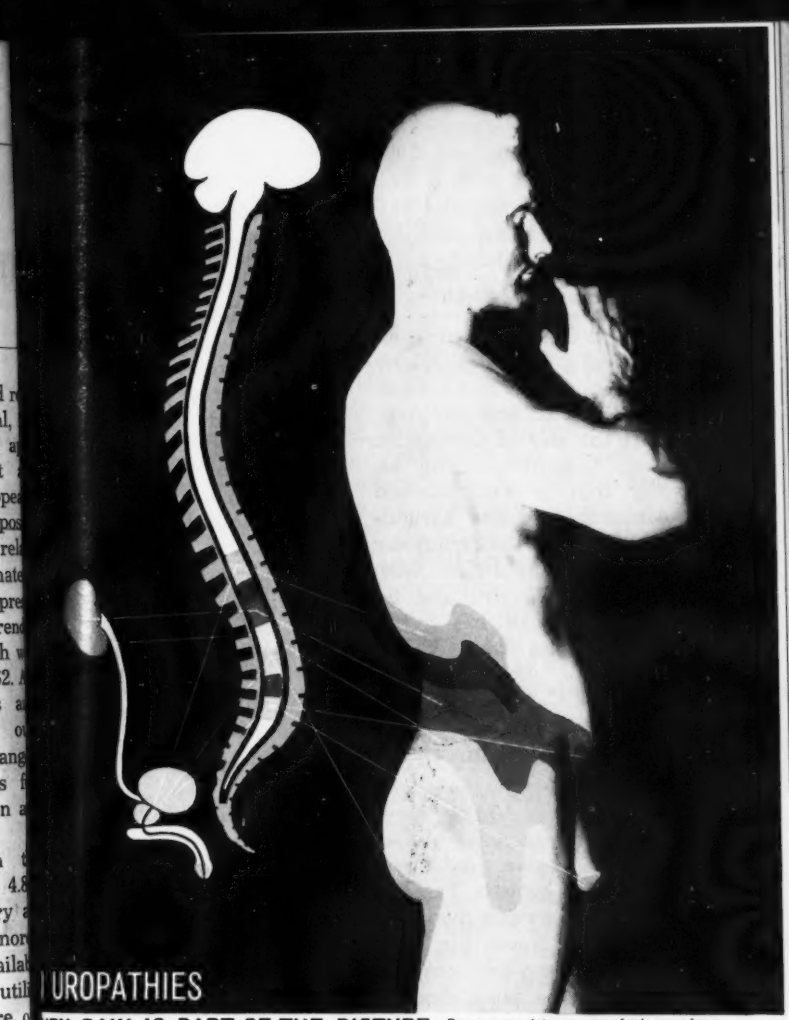
The electric power industry turned in an excellent performance last year. In spite of the prolonged steel strike, industry-wide kilowatt sales increased 9.8% above 1958, with revenues gaining about 8%. This year, sales are expected to rise about 9%, with revenues showing a further gain of something better than 7%.

	Current Price	Dividend	Yield	Estimated Value Range B.I.V.	G.V.
Cincinnati Gas & Electric	31½	$1.50	4.8%	31-36	36-42
Kansas City Power & Light	46½	2.20	4.7	47-55	54-63
Wisconsin Electric Power	37⅛	1.80	4.8	39-46	42-50
Wisconsin Public Service	25¾	1.30	5.0	25-29	31-37

In the selection of utility stocks for investment, we continue to think that those selling close to the low of carefully estimated value ranges offer the best opportunities for the long term. These are usually not the most popular stocks, as is indicated by the relatively high yields they provide at this time. By the same token, however, we believe that investors are getting good value for their money at current prices. The following issues, in our opinion, are reasonably valued and provide better-than-average income return at this time: Cincinnati Gas & Electric, Kansas City Power & Light, Wisconsin Electric Power and Wisconsin Public Service.

All of the issues selected for discussion this month are selling either at the lower level or slightly below our estimate of Basic Investment Value (See Table). Since this range represents our estimate of value based on a "full" overall return on the company's present investment, after deducting full annual interest and preferred dividend r quirements on senior capital, represents a "defensive" a praisal and indicates that present levels the stocks appe to enjoy a good defensive po tion with the downside risk rel tively limited. Our Estimate Growth Value is based on pre ently indicated growth tren and an earnings level which w think can be reached in 1962. A present prices the stocks a selling sufficiently below o projected Growth Value Rang to indicate that prospects f moderate price appreciation a favorable.

The average yield on t stocks in the above list is 4.8 compared with an industry a erage of 4.1% and the inor nately low 2.5% yield availab on a group of five notable utili growth stocks. Furthermore, o projections indicate that by 19 the average return on curre investment in the recommend stocks should increase to bet than 5.8%. On a price-earnin basis the stocks are selling at l



UROPATHIES

HEN PAIN IS PART OF THE PICTURE

nary tract pain, at the source or referred, is subject the rapid analgesic action of the azo dye in Azo trisin. Azo Gantrisin combines dramatic relief of symp- s with proven effective action against infections ried by either blood stream or urine.

uable also following urologic manipulation and surgery.

Diagram correlates sources of primary urinary pain with areas of referred pain

Dosage: Adults—2 tablets four times daily.
Children under 100 lbs—1 tablet four times daily.
Each tablet provides 0.5 Gm Gantrisin plus 50 mg phenylazodiamino-pyridine HCl—bottles of 100 and 500.

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than 15 times estimated 1959 earnings compared with a 17.2 times industry average and 25.6 times currently being paid for the five growth stocks.

Cincinnati Gas & Electric

Cincinnati Gas & Electric supplies natural gas and electricity to a population of almost 1.5 million in Cincinnati and environs, including the city of Covington, Kentucky. Encompassing an economy that is well-balanced between industrial and agricultural activities, the company serves 326 communities with electricity and 75 with gas. In addition, Cincinnati has a 9% stock interest in Ohio Valley Electric Corp., which supplies power to A.E.C. plants in Ohio and is active in projects to produce electricity from atomic sources.

The Ohio River Valley, serviced by the company, is undergoing considerable industrial and population growth. To meet the expanding service demands, the company in November, 1959, placed in service a new propane gas plant with a peak day capacity of 50 million cubic feet and is building a 165,000 kilowatt electric power unit for service in 1961. When added to its present capacity of three steam plants which have a capacity of 1,060,000 kilowatts plus the 165,000 kilowatts provide by a generating unit placed o line in July, 1958, the compan should be in a good position t keep pace with increasing d mand for electrical power.

Unlike other industries whos profits are determined by th price a company sets on its pro ucts, the price of utility com panies' "product" is regulated b state and Federal agencies. Rat in Ohio are negotiated direct with the municipalities, subje to the Ohio Public Utilities Com mission, and are regulated b the commission in unincorp rated areas. In Kentucky, th State Public Utilities Commi sion regulates the rates. Prope ties for rate-making purpos are evaluated at reproducti cost new depreciated in Oh and at net investment value Kentucky.

In mid-1959, the company n gotiated a gas rate increa which would increase annu revenues by about $250,000. A plication for a $2.24 million a nual increase in non-ordinar electric rates is currently pen ing before the Public Utilit Commission of Ohio. In additio negotiations for a $535,000 i crease in electric rate ordinanc have been proposed and subsid ary rate increases totaling abo $1.8 million annually have be put into effect, subject to refun

CINCINNATI GAS & ELECTRIC

Price	$31½
Dividend	$1.50
Yield	4.8%
Traded	N.Y.S.E.
1959-60 Price Range	30¾-37

Capitalization

Long Term Debt	$139,500,000
Cum. Preferred Stock ($100 Par)	
$4 Series; red. at $108	270,000 shs.
$4.75 Series; red. at $106 through Mar. 31, 1963, then less	130,000 shs.
Common Stock ($8.50 Par)	7,665,705 shs.

All told the proposed increases amount to about $4.8 million.

Revenues last year showed a favorable increase over 1958, but reflecting the pressure of sharply increased costs, earnings showed only a moderate improvement rising to $1.96 a share, as against $1.85 in 1958. The outlook for 1960, however, is more favorable as a result of the company's efforts toward obtaining rate relief. Assuming it receives a substantial portion of the proposed rate increases, earnings in 1960 should be about $2.00 a share. By 1962, it is reasonable to expect an earnings level of about $2.45 a share on about 5% more shares expected to be outstanding and we use this as the basis of our Growth Value estimate of 36 to 42.

Cincinnati Gas & Electric's dividend policy in the 1948-58 period has been to pay out around 62% of available earnings. Payments on its common stock have been made since 1953 and are currently set at $1.50 annually. Our projections indicate that by 1962 it is reasonable to anticipate dividends at an annual rate of $1.80 a share, a potential return of 4.8% on the present price. At a current price of 31½, which is 15% below its 1959-60 high of 37, the stock is selling at 16.6 times estimated 1959 earnings and 14.3 times our 1960 earnings estimate.

Kansas City Power & Light

Kansas City Power & Light provides electricity for Kansas City, Missouri, and several nearby communities in Missouri and Kansas. While the economy of the area is dependently mostly on corn, grains, livestock and dairying, Kansas City is also an important seat of auto assembly and steel manufacturing. Such companies as General Motors, Armco Steel, and Western Electric have recently built plants in the area. Other important customers include a new state hos-

pital, a guided missile base, and a new finishing plant of Missouri Portland Cement. In addition to supplying electricity, the company also provides steam service to the downtown business district of Kansas City, Missouri.

In an effort to expand the number of industrial and residential customers, the company set up an Industrial Development Department in 1958. The department works with other local development agencies as well as directly with other prospects who may be considering location or expansion in the service areas. The company also has engaged a research institute to make analysis of the industrial potential of its service area in order to obtain information for attracting new industries and in promoting expansion of existing industries.

Anticipating that there will be a steadily increasing demand for electricity in the near future, Kansas City Power & Light is nearing completion of the second of two new power plants. The first 175,000-kilowatt electric generating unit at the company's new Montrose Station was placed in service on July 16, 1958. The coal burned at this power plant about 60 miles southeast of Kansas City is obtained from strip mines in the immediate vicinity, which makes important savings in fuel cost

Work is in progress on a second 195,000-kilowatt unit, which is scheduled to be in service this spring. Completion of the new generator will increase the system's total capacity to 1,075,20 kilowatts. Since this will b about 38% above the company' 1959 summer peak load, no addi tional production facilities prob ably will be needed until 196 or later.

However, the company ha taken steps to insure that dur ing periods of peak demand, i will be able to supply electricity without taxing present facilities In late 1958, the firm entered into a contract with the South western Power Administration the marketing agency for the Federal Government power pro ject in southern Missouri, north ern Arkansas, and eastern Okla homa. The contract will enable the company to purchase hydro electric power for delivery prin cipally in the summer to meet added demand during the ho months.

Beginning June 1962, 75,00 kilowatts will be purchased from the SPA and, if required, the company may also purchase en ergy for emergency service. The contract runs until June 30 1987. However, either party can reduce the contract demand on 48 months' notice, but not prior

Tastefully tailored to the antibiotic needs of pediatric patients

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oxytetracycline with glucosamine

Delicious in taste: the appealing flavor of sweet, fresh fruit

Decisive in action: the well-tolerated broad-spectrum efficacy of Terramycin® with glucosamine

Preconstituted for uniform potency, efficacy, and taste-appeal from the first dose to the last.

Cosa-Terrabon Oral Suspension – 125 mg. oxytetracycline/5 cc., 2 oz. and 1 pint bottles

Cosa-Terrabon Pediatric Drops – 100 mg. oxytetracycline/1 cc., 10 cc. bottle with plastic calibrated dropper

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Pfizer *Science for the world's well-being*™

KANSAS CITY POWER & LIGHT

Price	$46½	Traded	N.Y.S.E.
Dividend	$2.20	1959-60 Price Range	45⅜-57½
Yield	4.7%		

Capitalization

Long Term Debt	$109,047,000	$4.35 Series; red. at $103½ through Apr. 30, 1962, then less	120,000 shs.
Cum. Preferred Stock ($100 Par):		$4.50 Series; red. at $102¼ through Mar. 1, 1962, then less	100,000 shs.
$3.80 Series; red. at $103.70	100,000 shs.	Common Stock (no par)	2,695,000 shs.
$4.00 Series; red. at $102¼	75,157 shs.		
$4.20 Series; red. at $103½ through Feb. 28, 1964, then less	70,000 shs.		

to December 31, 1963. This additional power will also enable the company to defer temporarily the construction of additional electric generating facilities. Accordingly, a 175,000-kilowatt unit planned for 1962 will be postponed possibly two years with consequent saving in capital charges.

Residential-rural sales provided 35% of electric revenues in 1958, and commercial-industrial 58%. Average domestic electric rates at 3.16¢ per kwh and annual usage of 2,863 kwh compared with 2.53¢ and 3,366 kwh nationally.

Also, the company's new money requirements during the next three years are moderate and no new financing will be required until 1962, when it is expected that debt will be sold. No equity financing is expected until 1963, or possibly 1964. In the absence of equity financing, a steady upward revenue trend may be expected to be reflected in increasing per share earnings and dividends. Last year earnings were equal to $3.10 a share compared with $3.05 in 1958. We estimate 1960 earnings at about $3.25 a share and 1962 earnings at approximately $3.75. Assuming the sale of moderate amount of common stock in 1963, this level of earnings should be maintained and would be somewhat higher if common stock financing is deferred until 1964.

Currently, the annual dividend is being paid at a $2.20 rate. However, earnings at the level projected would, in our opinion, support a dividend of $2.60 a share, giving a potential yield of 5.6%. The stock at $46½ is selling at its 1959-60 low, or

approximately 19% below its high for the period, and in our opinion, represents a good value.

Wisconsin Electric Power

Serving a population of approximately 1.71 million, Wisconsin Electric Power Company and its subsidiaries, Wisconsin-Michigan Power Company and Wisconsin Natural Gas Company, comprise an integrated power company providing customers with electrical energy, natural gas and, to a smaller extent, steam for heating. Besides its public utility business, the company operates electrical appliance stores in some nine cities. Approximately 87% of total revenues come from electric power, 11% from gas and 2% from heating and other business.

Its territory embraces some 4,000 square miles in the state of Wisconsin and the upper peninsula of Michigan, and includes prime industrial locations, the most important of which are Milwaukee and Milwaukee County. Although Milwaukee is a highly industrialized area, its industries are well balanced, consisting of heavy machinery, motor vehicle bodies and parts, lumber and paper companies, meat packing and malt drinks. In 1958, sales to industrial customers accounted for almost one quarter of the company's revenues.

Balancing the industrial load is a prosperous and stable agricultural community. In the southern part of the territory are rich farm lands, including some of the country's best dairy lands. The central district is also abundant in prosperous farm areas and contains important paper mills. At the close of 1958, the company was serving almost 99% of all the farms in its service area and the remaining farms had access to its distribution lines. Some idea of the relative prosperity of the area can be seen in the increased use of electricity over the past decade by residential and farm customers. During that period, the area's consumption rose more than 20% faster than the industry as a whole. In 1958, the national average usage of electricity stood at 3,366 kilowatt hours annually, compared to 3,617 kilowatts consumed by each of Milwaukee's customers.

Through membership in Atomic Power Development Associates, the company is taking part in studies related to the use of atomic energy for the production of electric power. In 1955, the company became one of 25 member companies of the Power Reactor Development Company and is contributing toward the

cost of building and operating a fast breeder power reactor plant on the west shore of Lake Erie. Construction has proceeded satisfactorily and initial operating tests are expected to begin some time this year.

As to its present generating power using conventional methods, its electric generating facilities consist of six steam-electric generating stations with an aggregate capacity of 1,317,500 kilowatts and one hydroelectric plant with a capacity of 240 kilowatts. Late in 1959, the company added another generating unit at its Oak Creek station, the largest of the system which has a rated capacity of 275,000 kilowatts and increased total system capacity to 1,650,610 kilowatts.

On August 1, 1958, the Public Service Commission of Wisconsin allowed an increase in electric rates sufficient to provide additional revenues of $3,816,000 annually. Additionally, the Commission found revenues from the sale of electric energy to the company's subsidiary, Wisconsin-Michigan Power Company, to be deficient by about $473,000 annually. In May, 1959, Wisconsin-Michigan Power applied for increased rates in Michigan, and in July asked the Federal Power Commission for increased rates for wholesale service to eight municipal systems and two public utilities. In addition, the parent company applied to the FPC for increased rates for certain wholesale services.

While the increases that were granted in the summer of 1958 contributed somewhat to earnings that year, the company's full year report showed net equal to $2.10 a share, the lowest since 1954, when the company earned $2.09 a share. However, the decline in earnings during 1958 was sharply reversed last year, largely as a result of the rate increase. For the full year, earnings improved to a total of $2.87, the highest on record. Assuming that the growth continues in line with indicated trends, our projections are that by 1962 an earnings level of at least $2.95 a share is a reasonable expectation and we use this as the basis for our Growth Value Range of 42 to 50.

The company's dividend policy has been to pay out about 70% of earnings. During the first three quarters of 1959, payments averaged 42½¢ a share plus a 10¢ year-end extra. With the March payment, however, the quarterly was increased to 45¢ a share. If this present policy is continued the dividend could reach a level of $2.20 annually by 1962. The yield on this dividend based on a current

reaches all nasal and paranasal membranes *sys emically*[1]

Pharmacologically balanced formula for prompt symptomatic relief

- in nasal and paranasal congestion
- in sinusitis and postnasal drip
- in allergic reactions of the upper respiratory tract

Triaminic*[2,3] *is safer and more effective than topical medication

- transported systemically to *all* respiratory membranes
- provides longer-lasting relief
- presents no problem of rebound congestion
- avoids "nose drop addiction"

Relief is prompt and prolonged because of this special timed-release action:

first— the outer layer dissolves within minutes to produce 3 to 4 hours of relief

then— the core disintegrates to give 3 to 4 *more* hours of relief

Each Triaminic timed-release Tablet provides:

Phenylpropanolamine HCl	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

Dosage: 1 tablet in the morning, midafternoon and at bedtime. In postnasal drip, 1 tablet at bedtime is usually sufficient.

Each timed-release Triaminic Juvelet® provides: **½ the formulation of the Triaminic Tablet.**

Dosage: 1 Juvelet in the morning, midafternoon and at bedtime.

Each tsp. (5 ml.) of Triaminic Syrup provides: **¼ the formulation of the Triaminic Tablet.**

Dosage (to be administered every 3 or 4 hours): *Adults* — 1 or 2 tsp.; *Children 6 to 12* — 1 tsp.; *Children 1 to 6* — ½ tsp.; *Children under 1* — ¼ tsp.

1. Fabricant, N. D.: E.E.N.T. Monthly *37*:460 (July) 1958.
2. Lhotka, F. M.: Illinois M. J.: *113*:259 (Dec.) 1957.
3. Farmer, D. F.: Clin. Med. *5*:1183 (Sept.) 1958.

the leading oral nasal decongestant...

Triaminic®

timed-release tablets and juvelets
also non-alcoholic, fruit-flavored syrup

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska

WISCONSIN ELECTRIC POWER

Price	$37⅛
Dividend	$1.80
Yield	4.8%
Traded	N.Y.S.E.
1959-60 Price Range	40½-35⅛

Capitalization

Funded Debt	$190,935,202
Cum. Preferred Stock ($100 par):	
$3.60 Series; red. at $102 through July 1, 1961; then $101	260,000 shs.
$6 Series; non-redeemable	44,508 shs.
Common Stock	5,608,270 shs.

price of 37⅛ would be 5.9%. At this price the stock is considered an attractive commitment.

Wisconsin Public Service

Wisconsin Public Service is engaged primarily in furnishing electric power and light service in northcentral and northeastern Wisconsin, and extending into Menominee County, Michigan. The territory, covering approximately 10,000 square miles, has an estimated population of 548,000. Electricity is sold at retail in 279 communities and at wholesale for redistribution by principal communities served, including Oshkosh, Green Bay, and Wausau. The urban territory is well diversified industrially, important economic factors including the manufacture of paper, machinery, metalware, furniture, electrical equipment, leather goods, food products, lumber and wood products. A number of port facilities are located on Lake Michigan and Green Bay. The surrounding rural area embraces important agriculture, dairy, and resort regions.

In addition to electric service the company sells manufactured gas in three communities in Wisconsin: Stevens Point, Peshtigo and Marinette; and Menominee, Michigan. Changeover from manufactured gas was completed in 1950, and natural gas now is sold in 15 communities (88% of all customers). The company also owns one-third interest in Wisconsin River Power Co., and owns 39.1% voting stock of Wisconsin Valley Improvement Co., which maintains a system of reservoirs regulating flow of the Wisconsin River.

In 1958, electricity provided 78% of revenues, gas 21% and transportation about 1%. Residential sales accounted for 24% of electric gross, rural 19%, commercial 13% and industrial 32%. Average domestic electric

WISCONSIN PUBLIC SERVICE

Price	$25¾	Traded	O.T.C.
Dividend	$1.30	1959-60 Price Range	23¼-27½
Yield	4.1%		

Capitalization

Funded Debt	$63,782,000	less	30,000 shs.
Cum. Preferred Stock ($100 par):		$5.08 Series; red. at $107 through October 31, 1963, then less	50,000 shs.
$5.00 Series; red. at $107.50	132,000 shs.	Common Stock: ($10 Par)	2,788,431 shs.
$5.04 Series; red. at $104.81 through May 1, 1963, then			

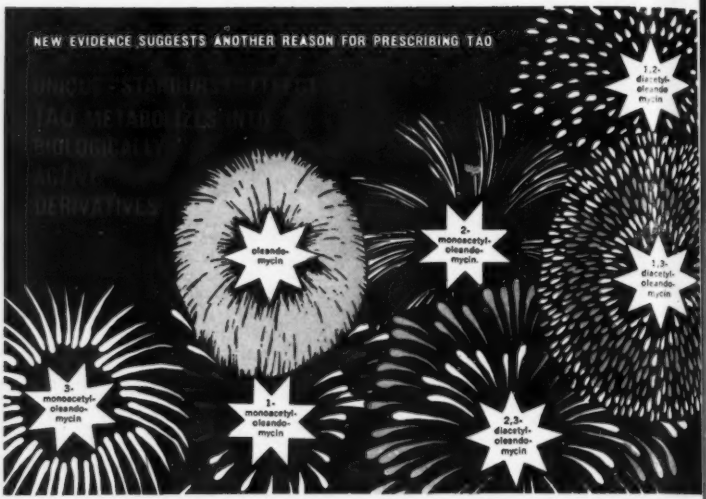
rates at 2.56¢ per kwh and annual usage of 3,260 kwh compared with 2.53¢ and 3,366 kwh nationally.

Generating capacity on December 31, 1958, totaled 415,463 kw., of which 63,296 kw. was hydro, and 11,667 kw. represented a one-third interest in power produced by the Wisconsin River Power hydro plant.

Year-to-year revenue fluctuations have generally been relatively narrow, reflecting the diversified nature of the service territory. Gross declined only 7.5% in the 1932-33 depression, then expanded steadily through 1958. Although the earnings record was much less stable, net in 1958 was at an all-time peak.

At its current price of 25¾, the stock is selling at 13.5 times 1959 earnings of $.90 per share, up from $1.77 in 1958. Growth in the company's area is continuing at a favorable level, and we estimate that the earnings trend will continue upward. As a result of recent favorable developments in the matter of obtaining additional gas supplies, the company has been able to increase the number of its space heating customers.

Over the longer term, final approval of the export of Canadian gas should enable the company to further expand its gas business. Although it will be necessary to sell additional stock during the next few years, projections indicate that by 1962, earnings could reach $2.20 a share, on which basis we believe the stock has a growth value in the range of 31 to 37. Assuming a $2.20 earnings level, a dividend of $1.60 per share would appear to be a reasonable expectation. This would afford a yield of about 6.2% on the present price.◀



The impression that TAO is an unusually active antibiotic has steadily gained recognition by impressive clinical performance. Now come reports of *in vivo* and *in vitro* biological and biochemical evaluations that show TAO to be indeed unique.[1,2]

TAO differs from other antibiotics in that it is metabolized to multiple active compounds which remain active throughout their presence in the body. These 7 derivatives (as well as TAO) show activity against common Gram-positive pathogens, including resistant strains of *Staph. aureus*.

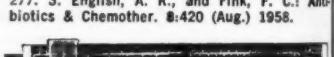
In light of these findings, take another look at TAO performance: • 92% success in published cases of Gram-positive respiratory, skin, soft tissue and genitourinary infection • Effective against 78% of 64 "antibiotic-resistant" epidemic staphylococci. (In the same study, chloramphenicol was active against 52%; erythromycin against only 25%)[3] • No side effects in 94%; infrequent reactions mild and easily reversed • Quickly absorbed • Highly palatable.

Sound reasons to: Start with TAO to end 9 out of 10 common Gram-positive infections.

Supplied: TAO Capsules—250 mg., and 125 mg., bottles of 60. **TAO for Oral Suspension**—125 mg. per tsp. (5 cc.) when reconstituted; unusually palatable cherry flavor; 60 cc. bottle. Prescription only.

Other TAO forms available: TAO Pediatric Drops: flavorful, easy to administer. **TAO®-AC:** TAO analgesic, antihistaminic compound. **TAOMIDE®:** TAO with triple sulfas. **Intramuscular or Intravenous:** in clinical emergencies. Prescription only.

1. English, A. R., and McBride, T. J.: Proc. Soc. Exper. Biol. & Med. 100:880 (Apr.) 1959. 2. Celmer, W. D.: Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959, p. 277. 3. English, A. R., and Fink, F. C.: Antibiotics & Chemother. 8:420 (Aug.) 1958.



designed for superior control of common Gram-positive infections

TAO®

(triacetyloleandomycin)

Capsules/Oral Suspension

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

►Decagesic Tablets
(Merck Sharp & Dohme)

Each tablet contains 0.25 mg. of dexamethasone, 500 mg. of aspirin and 75 mg. of aluminum hydroxide (present as the dried gel). *Indications:* For the management of patients with rheumatoid arthritis (including palindromic rheumatism), rheumatoid spondylitis, psoriatic arthritis, disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis, scleroderma, painful inflammatory musculoskeletal conditions such as bursitis, acute and chronic low back pain, synovitis and nonpurulent tenosynovitis. *Dosage:* One or two tablets 3 or 4 times daily. *Supplied:* In bottles containing 100 tablets.

►Mysteclin "F" Aqueous Drops *(Squibb)*

When reconstituted each cc. contains tetracycline equivalent to 100 mg. of tetracycline hydrochloride (potentiated with potassium metaphosphate) and 20 mg. of amphotericin B. *Indications:* For the treatment of mixed infections due to susceptible organisms. *Dosage:* Pediatric dosage should supply 10 to 20 mg. of tetracycline per pound of body weight each day in divided doses, depending on type and severity of the infection. *Supplied:* In 10 cc. bottles with dropper.

►Quelicin Chloride
(Abbott)

Succinylcholine chloride: 20, 25, 50, or 100 mg. per ml. *Indications:* For muscular relaxation in endotracheal intubation, endoscopic examination, orthopedic manipulation, general surgery, electroshock therapy and laryngospasm. *Contraindications:* Severe liver disease, severe anemia, severe malnutrition and insecticide poisoning. *Dosage:* To be determined on the basis of application. *Supplied:* In 20 ml. and 40 ml. vials containing 25 mg. per ml. In 10 ml. multiple-dose vials containing 20 mg. per ml. In 10 ml. ampuls containing either 50 mg. or 100 mg. per ml.

►Miradon Tablets *(Schering)*

Each tablet contains 50 mg. of anisindione. *Indications:* Oral anticoagulant. Therapeutically: Coronary occlusion with myocardial infarction, thrombophlebitis, arterial embolism or thrombosis, pulmonary embolism secondary to intravascular clotting, phlebothrombosis. Prophylactically: Traumatic injury to blood vessels, vascular surgery, pelvic and massive surgery, postpartum cases with history of thrombophlebitis. *Dosage:* To be given orally in a single daily dose. Initial doses are 300 mg. the first day, 200 mg. the second day and 100 mg. the third day. Maintenance dose should be individually determined and may vary from 25 mg. to 250 mg. daily. *Supplied:* In bottles containing 100 tablets.

►Librium Capsules *(Roche)*

Psychodynamic drug. Each capsule contains 10 mg. of the drug that is chemically 7-chloro-2-methylamino-5-phenyl-3H-1, 4-benzodiazepine 4-oxide hydrochloride. *Indications:* Whenever fear, anxiety and tension are significant components of the clinical profile. *Dosage:* To be adjusted to the needs of the patient. *Supplied:* In bottles containing 50 or 500 capsules.

►Analexin-AF *(Irwin, Neisler)*

Analgomylaxant. Each tablet contains 100 mg. of phenyramidol and 300 mg. of aluminum aspirin. *Indications:* For relief of pain and musculoskeletal tension associated with inflammatory processes and/or fever as in arthritis, arthralgia, bursitis, tendinitis, myalgia of strain and tear, and pre- and postoperative toothache. *Dosage:* Two tablets every 4 hours, or as required. *Supplied:* In bottles containing 100 tablets.

►Cosa-Terrabon Pediatric Drops *(Pfizer)*

Ready-to-use pediatric dosage form of the broad-spectrum antibiotic terramycin (as calcium di-oxytetracycline) with glucosamine (as N-acetylglucosamine). *Indications:* Infections caused by Gram-positive and Gram-negative bacteria, rickettsiae, spirochetes and large viruses, respiratory tract infections, genitourinary, ophthalmic, surgical, soft tissue, meningeal, dental, gastrointestinal and miscellaneous infections due to susceptible organisms. *Dosage:* Optimal dosage varies with severity, response and susceptibility of infection. *Supplied:* In 10 cc bottles with calibrated plastic dropper.

►Therabile Tablets *(Ascher)*

Digestant. The enteric-coated core contains 25 mg. of desoxycholic acid, 200 mg. of ferrated ox bile, 100 mg. of dl-methionine and pancreatin (4 x N.F.), 62.5 mg. (equivalent to pancreatin, N.F. 250 mg.). The outer layer contains 2.5 mg. of homatropine methylbromide and 1/600 grain of oleoresin of ginger. *Indications:* Noncalculous gallbladder disease and post-operative gallbladder disorders, and to support over-all digestive function. *Dosage:* One tablet three times daily. *Supplied:* In bottles containing 100 or 500 tablets.

►Delenar Tablets
(Schering)

Each tablet contains 0.15 mg. of dexamethasone, 15 mg. of orphenadrine hydrochloride and 300 mg. of aspirin (as aluminum salt). *Indications:* Mild cases of rheumatoid arthritis, mild or moderate spondylitis, subacute or interval gout, bursitis, low-back strain, synovitis, tendosynovitis, neuritis, shoulder-hand syndrome, non-specific low-back pain, torticollis and whiplash injuries. Atopic and contact dermatoses. *Contraindications:* Do not use in patients with active tuberculosis, peptic ulcer, agitated psychotic states or herpes simplex of the eye. Use cautiously in patients with glaucoma, tachycardia or urinary retention. *Dosage:* To be adjusted to the individual requirements of the patient and the condition being treated. *Supplied:* In bottles containing 100 or 1000 tablets.

►Sporostacin *(Ortho)*

White vaginal cream. The active ingredient is 1% chlordantoin. *Indications:* Fungus infections of the vulvovaginal area, particularly moniliasis (candidiasis) and in monilial overgrowth occurring during or after antibiotic therapy. *Dosage:* Apply to the affected area once or twice daily as required. *Supplied:* In plastic tubes of 95 gm. with or without vaginal applicator.

►Geriliquid *(Lakeside)*

Peripheral vascular dilator. Each 5 ml. teaspoonful contains 75 mg. of niacin and 750 mg. of glycine in a sherry wine base. *Indications:* For cold hands and feet, pain and other conditions due to poor peripheral circulation. *Dosage:* Usually one or two teaspoonfuls three times daily. *Supplied:* In bottles containing eight fluid ounces.

►Ornade Spansules *(S.K.F.)*

Each sustained-action capsule contains 2.5 mg. of isopropamide (as the iodide, 50 mg. of phenylpropanolamine hydrochloride and 8 mg. of chlorprophenpyridamine maleate. *Indications:* For symptomatic relief of nasal congestion in colds, allergies and associated conditions. *Dosage:* Adults and children over six years of age, one capsule every 12 hours. *Supplied:* In bottles containing 30 capsules.

►Cosa-Terrabon Oral Suspension *(Pfizer)*

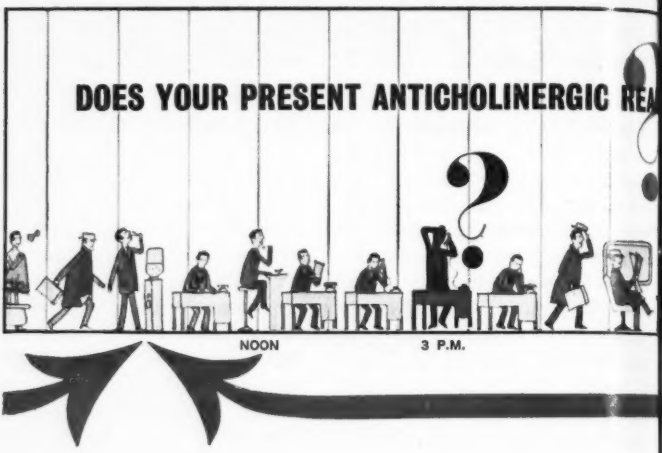
Each 5 cc. teaspoonful of preconstituted aqueous suspension contains calcium di-oxytetracycline equivalent to 125 mg. of oxytetracycline with 125 mg. of glucosamine as N-acetylglucosamine. *Indications:* Infections caused by Gram-positive and Gram-negative bacteria, rickettsiae, spirochetes and large viruses, respiratory tract infections, genitourinary, ophthalmic, surgical, soft tissue, meningeal, dental, gastrointestinal and miscellaneous infections due to susceptible organisms. *Dosage:* Optimal dosage varies with severity, response and susceptibility of infection. *Supplied:* In bottles containing 2 ounces of suspension.

►Mysteclin "F" for Syrup *(Squibb)*

Anti-infective. When reconstituted each 5 cc. teaspoonful contains tetracycline equivalent to 125 mg. of tetracycline hydrochloride (potentiated with potassium metaphosphate) and 25 mg. of amphotericin B. *Indications:* For treatment of mixed infections due to susceptible organisms, especially in patients susceptible to monilial overgrowth. *Dosage:* Pediatric dosage should supply 10 to 20 mg. of tetracycline per pound of body weight each day in divided doses, depending on type and severity of infection. Adults should receive a minimum of 250 mg. four times a day. *Supplied:* In 60 cc. bottles.

►pHisoAc Cream *(Winthrop)*

Dermatologic cream containing colloidal sulfur, 6%; resorcinol, 1.5%; hexachlorophene, 0.3%; orthophenylphenol, 0.3%; alcohol, 10% (w/w) in flesh-colored, greaseless base. *Indications:* For the topical treatment of acne. *Dosage:* Apply in a thin layer with a gentle stroking motion. Wash skin before use with antiseptic detergent. Leave on overnight. Patients with very oily skin may also use the cream during the day. *Supplied:* In 1½ ounce (42.5 gm.) tubes.



The test—you might say the acid test—of an anticholinergic is simple: will it protect your patient from hyperacidity around the clock, **even while he sleeps.** The weakness of t.i.d. or q.i.d. preparations is well recognized; but even some "b.i.d." encapsulations may be unreliable. McHardy, for instance, found a "widely variable duration of action, definitely less than that anticipated" in the "sustained," "delayed," and "gradual release" anticholinergics he studied.[1]

COMPARE THE DATA ON ENARAX . . . the new combination of an **inherently** long-acting anticholinergic (oxyphencyclimine) and Atarax, the non-secretory tranquilizer. Note the effectiveness of oxyphencyclimine:

OBSERVE THE OXYPHENCYCLIMINE REPORTS . . .

McHardy: "[Oxyphencyclimine] has proved to be an excellent sustained-action anticholinergic in our study of this agent over a period of eighteen months."[1]

Kemp: ". . . for the majority of patients, one tablet every 12 hours provided adequate control. This characteristic long action . . . may constitute an advantage of this drug as compared to coated 'long-acting' preparations of other compounds."[2]

Add Atarax to this 12-hour anticholinergic. The resulting combination—ENARAX—now gives relief from emotional stress, in addition to a reduction of spasm and acid. Atarax does not stimulate gastric secretion. No serious adverse clinical reaction has ever been documented with Atarax.

LOOK AT THE RESULTS WITH ENARAX[1-3]:

Does the medication you now prescribe assure you of all these benefits? If not, why not put your next patient with peptic ulcer or G.I. dysfunction on therapy that **does.**

ENARAX®

(oxyphencyclimine plus ATARAX®)

A SENTRY FOR THE G.I. TRACT

▶ Atlas of Roentgenographic Positions, Volume I and Volume II, Second Edition

by Vinita Merrill, formerly educational director, Picker X-ray Corporation. The C. V. Mosby Company, St. Louis 3. 1959. $32.50 for the two vols.

In addition to the elaborate expositions and illustrations of the first edition this book carries what has been learned in the meantime by experience and from a diligent survey of the relevant literature. It has been noted that valuable additions have been made to the positions, the assuming of which will give best exposures and therefore pictures which best supply information of greatest value. More than 40 of these positions, many new, have been added in the preparation of this work, while a number of the older ones have been replaced. Many of the sections have been rewritten, some of them completely. The terminology has had many changes in the interest of uniformity and clarity. Consideration is given to some of the idiomatic terms used especially by workers in this field in order to elucidate their meaning for those beginning this study. The advances made in the study of this form of diagnosis in the past decade, added to previous knowledge set forth in the first edition, make these two volumes a text on the subject second to none.

▶ Medieval and Renaissance Medicine

by Benjamin Lee Gordon, M.D., F.I.C.S., Philosophical Library, New York. 1959. $10.00

To the medical scholar and to a good many others this book will afford information of interest obtainable otherwise only by the expenditure of a great deal of time and effort, and travel in many countries. The English is of the first order, the illustrations interesting and revealing. The exceptional medical man will be much better entertained and informed in the perusal of these pages over many evenings than by having his eyes and ears assailed by the tommyrot of the television performances.

► Newer Concepts in Clinical Proctology

by Frank D. Stanton, D.O. Clinton Press, Inc., Clinton, Mass. 1958.

The writer of the foreword credits the author with having a special gift of making the complex simple, of perceiving at once the essence of his own special field, and presenting a method for use in proctology simply, essentially, and uniquely.

► Hypertension: The First Hahnemann Symposium on Hypertensive Disease

edited by John H. Moyer, M. D., Professor and Chairman of the Department of Medicine, Hahnemann Medical College and Hospital, with the assistance of John R. Beem, M.D., Robert Bower, M.D., Joseph R. DiPalma, M.D., Arthur Grollman, M.D., William Likoff, M.D. and Lewis C. Mills, M.D. W. B. Saunders Company, Philadelphia. 1959. $14.00

This monograph of nearly 800 pages, the work of some 80 authorities on this subject of first importance, is an exhaustive dealing with hypertension, under eight heads:

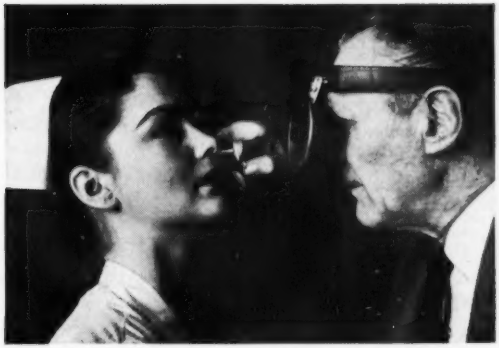
Pathology and Clinical Aspects, Basic Concepts of the Etiology, Pharmacology and Use of Sympathetic Blocking Agents, Role of Salt and Diuretics in the Therapy, Special Problems in the Therapy, Surgical Approach to Essential Hypertension, Effect of Therapy on Prognosis, and Recommendations for Drug Therapy.

The importance of this subject justifies the exhaustive preparation of this volume, all of which will amply repay the study of any clinician.

► Handbook of Diet Therapy, Third Edition

written and compiled by Dorothea Turner, Department of Medicine, University of Chicago, for the American Dietetic Association. The University of Chicago Press, Chicago. 1959. $5.00

Few will dispute that intelligent diet therapy should be molded around a basic food base plan selected to provide the essentials of good nutrition, yet with consideration of the disease the patient has and his food habits. Emphasis must be placed on the food habits of the individual these habits being based on personal inclination induced by wise nature. In health, and in most disease, nature is entirely reliable in her promptings as to what, how much, and how often we should eat. A book such as this supplies reliable guidance in the exceptional case.



EVEN HOT STAPH.* SUCCUMB TO

FURACIN® NASAL

brand of nitrofurazone

with phenylephrine

to conquer a growing problem—resistant staph.

"We have used FURACIN Nasal successfully in eradicating staphylococci from the nasal passages of our nursing personnel. The majority of cases are cleared with 5 days of treatment."[1]

routine in sinusitis, rhinitis and nasopharyngitis

"Intranasal and sinus infections have been found to disappear promptly . . . helps to combat the associated nasopharyngitis."[2]

■ wide bactericidal range ■ negligible bacterial resistance ■ no cross-sensitization or bacterial cross-resistance to systemic agents ■ low sensitization rate ■ no irritation, no stinging, no slowing of the ciliary beat ■ no interference with phagocytosis or healing.

FORMULA: FURACIN 0.02% with phenylephrine•HCl 0.25% in an aqueous, isotonic solution of sodium salts and methylparaben.

SUPPLY: Plastic atomizer of 15 cc. for administration by either spray or drop.

References: 1. Personal Communication to Eaton Laboratories, 1959. 2. Spencer, J. T., in Conn, H. F.: Current Therapy 1954, Philadelphia, W. B. Saunders Co., 1954, p. 130.

*antibiotic-resistant staphylococci

THE NITROFURANS—a *unique* class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK

► Acute Pericarditis

by David H. Spodick, M.D., Clinical Instructor in Medicine, Tufts University School of Medicine. Grune and Stratton, Inc., New York and London. 1959. $6.50

Since there is such a wide range in the seriousness of pericarditis and in its implications and complications, it is deserving of more extended consideration than is comonly given it in texts of Medicine or even Cardiology. Here is the book.

► Proceedings of the World Congress of Gastroenterology and the Fifty-Ninth Annual Meeting of the American Gastroenterological Association

The Williams & Wilkins Company, Baltimore. 1959. $20.00 for the two volumes.

Our own great authority in this field, Dr. H. L. Bockus, served as Chairman of this Congress. He says in the Foreword, "In the pages of these two volumes will be found a record of the scientific deliberations of the . . . Congress . . . The contributions emanate from physicians and scientists of distinction from all parts of the world."

Inaugural speakers discussed broad subjects, such as The Ulcer Problem, Medical and Social; Progress and Change in Gastroenterology; The Role of the Surgeon in the Development of Gastroenterology as a Specialty; and Electronics and Biology. These speakers were followed by some hundreds of teachers and investigators and gastroenterologists in private practice, who brought to the meeting all the reliable knowledge on this subject that the world holds. Though retired from practice as an internist, and never having paid any special attention to gastroenterology, this reviewer has read with great pleasure the offering on Peptic Ulcer by Dr. Sara M. Jordan. It is too much to promise the reader that the two volumes are made up of articles as lucid and erudite as the article of Dr. Jordan, but promise can be made that all the useful knowledge of the subject that is extant will be found.

► Master Your Tensions and Enjoy Living Again

by George Stevenson, M.D. and Harry Milt. Prentice-Hall, Inc., New York. 1959. $4.95

A popular approach to a popular subject which will be welcomed, read, and discussed by many enthusiasts.